Multiple Stressors Conference – Novel Methods for Integrated Risk Assessment

Proceedings

Aarhus, 28 - 30 September, 2009

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DATA SHEET

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Abstract:	The proceedings are a compilation of abstracts of presentations and introductions given at the Multiple Stressors Conference – Novel Methods for Integrated Risk Assessment. These abstracts are both from platform presentations and posters.
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Preface

This conference was the sixth and final NoMiracle Conference. The meeting was open for contributions from other activities in the area, and it was organised in collaboration with the PHIME project. It was the aim that a broad array of leading scientists in the area of impact of multiple stressors on environment and health, in particular chemical mixtures, would meet and share their latest results and progress with scientists from NoMiracle and PHIME.

This meeting was prepared by the NoMiracle Secretariat in Silkeborg. I would like to thank for all their hard work: Lene Birksø, Charlotte Kler and Morten Strandberg. I also acknowledge the work done on graphic design and layout by Juana Jacobsen. I enjoyed working with the Scientific Committee counting Dorota Jarosinska, Peter van den Hazel, Peter Pärt, Ad Ragas, Gerrit Schüürmann, Dave Spurgeon, and Jürg Oliver Straub, and I highly appreciate the contributions from PHIME by Staffan Skerfving and from Mikael Hildén and Timo Assmuth on the session on risk concepts and governance.

It is my hope that this meeting will facilitate and contribute to the current development of tools for coping with the difficult risk assessment of multiple stressors for man and the environment.

Hans Løkke

NoMiracle Coordinator

Introduction to the programme

The programme was organised in plenary sessions, parallel sessions and poster sessions. The sessions were grouped on topics which joined human health and ecological aspects of exposure, effects and risk assessment of multiple stressors. The programme contained presentations from a large array of scientists, among these were participants from the FP6 projects NoMiracle and PHIME.

The NoMiracle project (http://nomiracle.jrc.ec.europa.eu) under the European Sixth Framework Programme FP6, Global Change and Ecosystems, involves thirty-eight institutions from 17 countries and counts 200 persons working together for 5 years (2004-2009) on the development of better methods to analyse, characterise and quantify the combined risks to health or the environment from multiple stressors. Examples of such cumulative stressors are mixtures of chemicals alone or in combination with biological or physical environmental factors such as pathogens and climatic conditions.

The Main Science & technology objectives of the project are

I. To develop new methods for assessing the cumulative risks from combined exposures to several stressors including mixtures of chemical and physical/biological agents

II. To achieve more effective integration of the risk analysis of environmental and human health effects

III. To improve our understanding of complex exposure situations and develop adequate tools for exposure assessment

IV. To develop a research framework for the description and interpretation of cumulative exposure and effect

V. To quantify, characterise and reduce uncertainty in current risk assessment methodologies, e.g. by improvement of the scientific basis for setting safety factors

VI. To develop assessment methods which take into account geographical, ecological, social and cultural differences in risk concepts and risk perceptions across Europe

VII. To improve the provisions for the application of the precautionary principle and to promote its operational integration with evidence-based assessment methodologies

The Consortium counts scientists within human toxicology and epidemiology, aquatic and terrestrial ecotoxicology, environmental chemistry/biochemistry, toxicogenomics, physics, mathematical modelling, geographic informatics, and socio-economic science.

The PHIME (Public Health Impact of long-term, low-level Mixed Element exposure in susceptible population strata) Project (www.phime.org) under the European Sixth Framework Programme FP6, Food quality and safety, involves 35 partners from 22 countries working together for 5 years (2006-2011). The project covers a broad range of multiple stressor aspects.

PHIME´s operational goals are in brief to respond to three major questions:

I. What are the problems?

I.1 Nervous system: Impact of elements (mercury, arsenic, manganese, lead) on the developing and adult nervous system. Are there gene-environment and nutritional interactions?

I.2 Cardio- and cerebrovascular disease: Impact of elements (mercury, selenium). Gene-environment and nutritional interactions

I.3 Skeleton: Impact of cadmium (osteoporosis, fractures). Interactions with genes and other environmental pollutants (persistent organochlorines)

I.4 Kidney disease and diabetes: Impact of elements (cadmium, lead, mercury)? Gene-environment interaction

II. Where are the problems?

II.1 Biomarkers: Strategies for sampling (lead, cadmium, mercury, platinum, palladium, rhodium)

II.2 Geographical patterns of exposure

II.3 Time trends of exposure

III. Possible solutions of the problems (some)?

III1 Plant sciences: Mechanisms of transport of elements (cadmium, zinc) in plants.

III.2 Risk assessment of human exposure (cadmium, mercury, lead).

The PHIME Consortium gathers more than 100 senior scientists in environmental and occupational medicine, toxicology, molecular biology, nutrition, epidemiology, biostatistics, analytical chemistry and plant sciences.

In Aarhus, a broad array of important new findings and novel approaches in risk assessment were presented and discussed. The conference was opened by the Rector of Aarhus University, Dr. Lauritz B. Holm-Nielsen, and introduced by the NoMiracle Coordinator, Dr. Hans Løkke. The first plenary session set the stage by keynote lectures on “Protecting human health and ecosystems – connecting novel research, practice and policy on multiple stressors”, “Human variability in toxicokinetics, chemical mixtures and uncertainty factors for chemical risk assessment”, and “Multiple Stressors – Novel Methods for Integrated Risk Assessment: viewpoints from European chemicals industry”.

The first conference day included two parallel sessions on important issues

1: Combined effects of natural stressors and chemicals, and

2: New concepts and techniques in fate and exposure assessment

Among the presentations, scientists from NoMiracle have succeeded in making a first step towards assessment of the combined impact of natural stressors and chemicals. Both sessions presented a variety of tools and concepts.

The second day dealt with chemical mixtures in parallel Session 1. The topic was introduced by an outline on how to apply a systematic biological approach in the description and prediction of mixture effects. A series of presentations ranged from testing with human immune cells to full-scale ecological assessment of cumulative stressors, and current trends and critical aspects were discussed.

The results from the PHIME project were presented on the second day in parallel Session 2 entitled “Risk of mixed exposures to metals”.

Parallel Session 2 on the second day dealt with integrated risk concepts and governance. Special attention was paid to cumulative stressors.

The second day was closed by a poster session, allowing for short platform presentations and poster corners around thematic groups of posters covering ecological as well as human health risks. These groups included:

- Chemical fate and exposure
- Effects of mixtures of chemicals and combinations of chemicals and other stressors
- Cumulative risks in complex systems
- Risk perception, risk communication and assessment-governance links

The third and last day started with parallel sessions on:

1: New concepts and techniques for risk assessment

2: Risk presentation and visualisation

Besides presentations on ecosystem services and toxicity profiling, the parallel Session 1 included presentations on uncertainty, which is crucial in risk assessment. Parallel session 2 described tools for visualising risks to man and environment, and was closed by a presentation of one of the NoMiracle Master Cases, demonstrating new tools for risk assessment.

The theme of uncertainty and ambiguity was dealt with in a world café, involving all conference participants in an active process, potentially winding up in a set of recommendations.

The conference was crowned by a panel discussion on strategies for testing and risk assessment of multiple stressors. How to implement their findings in regulatory practise is an outstanding question for all large EU-projects like NoMiracle and PHIME. Is a shift of paradigm and change of test guidelines possible? In the case of NoMiracle, marked advances, reduced uncertainty and even less testing may be

obtained by introducing novel methods in guidelines for current risk assessment such as distinct characterisations of compound-matrix interactions in terms of H-bounding QSAR prediction and chemical activity assessment, and prediction of mixture toxicity in time using Dynamic Energy Budget-based approaches. Giving a scientific background, the panel discussion was introduced by short communications from leading scientist in fields which open for new and better tools which require changes of current practice.

This conference was the sixth and final open international meeting organised by NoMiracle. Former NoMiracle workshops were:

1. "Ecological and Human Health Risk Assessment: Focussing on complex chemical risk assessment and the identification of highest risk conditions", 1st open international NoMiracle workshop, Verbania - Intra, Italy June 8-9 2006. Proceedings: Pistocchi, A. (ed.) http://nomiracle.jrc.ec.europa.eu/

2. "Communicating chemical risks" 2nd open international NoMiracle workshop, The International Meeting Centre of the University (IBZ), Stuttgart, Germany. Proceedings: Benighaus, C; Renn, O. (eds) http://nomiracle.jrc.ec.europa.eu/webapp/ViewPublicDeliverables.aspx

3. "Novel Methods for Assessing Chemical Exposure for the 21st Century", 3rd open international NoMiracle workshop, Leipzig, Germany, 1-2 April, 2008. Report: Cousins, I; Mayer, P. NoMiracle Newsletter 12, 1-4

4. "Integrated Assessment of Environmental and Human Health", 4th open international NoMiracle workshop, Frankfurt, Germany, 8-9th September 2008. Report: Spurgeon, D.; Løkke, H. NoMiracle Newsletter 13, 10-13.

5. "Cumulative Risk Assessment: a Challenge for Science and Management", 5th open international NoMiracle workshop, Ravenstein, The Netherlands, 26-27 March 2009.

Keynote Presentations

Protecting human health and ecosystems – connecting novel research, practice and policy on multiple stressors

Dr. Dorota Jarosinska, European Environmental Agency (EEA), Denmark

Human variability in toxicokinetics, chemical mixtures and uncertainty factors for chemical risk assessment

Dr. Jean-Lou Dorne, European Food Safety Agency (EFSA), Italy

Multiple Stressors – Novel Methods for Integrated Risk Assessment

Dr. Bruno Hubesch, European Chemical Industry Council (CEFIC), Belgium

Protecting human health and ecosystems – connecting novel research, practice and policy on multiple stressors

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SUMMARY

There is a growing recognition of complexity of interactions between the environment and human health, with both humans and ecosystems being challenged by many stressors. Risk assessment of individual chemicals and measures targeted at specific environmental issue can help reduce burden, but are not sufficient to effectively protect human health in a changing environment. For hazardous chemicals, such as heavy metals, endocrine disrupting substances and other persistent, bioaccumulative compounds, evidence emerges on potential impacts of exposure to mixtures, even at low levels, especially in vulnerable populations. Novel methods and approaches in exposure/fate assessment, cumulative risk assessment, mixture toxicology, vulnerability analysis, etc., are crucial to progress the knowledge of potential impacts, which might be indirect, distant (in terms of space and time), non-specific, modified by different vulnerability and other conditions (e.g. socio-economic) and highly uncertain. Applicability of a system based approach, taking into account thresholds, nonlinearity, feedback loops, and time lags might be explored in this context. Improved understanding of the nature and potential effects of exposure to mixtures of hazardous pollutants and to other stressors, together with refined assessment of vulnerabilities (of a population, location, ecosystem) can help to better adjust responses and preventive measures, as well as to explore possible co-benefits. Given multicausal nature of possible associations, difficulties in establishing a cause-effect chain, and uncertainty, efforts are needed to further develop 'anticipatory and precautionary approaches' to addressing such complex issues, and for adequate communication.

Human variability in toxicokinetics, chemical mixtures and uncertainty factors for chemical risk assessment

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SUMMARY

A 100-fold uncertainty factor (UF) has been used for the last forty years to set health based guidance values for non-genotoxic carcinogens. This UF allows for interspecies differences and human variability and subdivision for the toxicokinetic and toxicodynamic aspect have been proposed with even values of $10^{0.5}$ (3.16) for the human aspect. Such refinements allow for chemical-specific adjustment factors (CSAF) and physiologically-based models to replace such default UFs. An intermediate option between default UFs and CSAFs are pathway-related UFs. The development of of pathway-related UF is illustrated here through the incorporation of variability data in toxicokinetics, including analysis of subgroups of the population (poor metabolisers in the case of genetic polymorphisms, neonates, children, the elderly…) for the major metabolic routes in humans (phase I, phase II metabolism and renal excretion). In addition, the use of Latin hypercube (Monte Carlo) models using quantitative metabolism/toxicokinetic data and pathway-related lognormal variability for the prediction of toxicokinetic variability and UFs for compounds handled by several metabolic routes are discussed. Within the context of NOMIRACLE, two other additional aspects are described: (1) the harmonisation of the use of UF for human and ecological risk assessment (2) the analysis of toxicokinetic interaction data in humans for polymorphic routes of metabolism (CYP2D6, CYP2C9, CYP2C19) to provide assess the validity of default UFs for mixtures

Conclusions and recommendations on the use of toxicokinetic data in risk assessment are discussed together with particular emphasis on the use of sound statistical approaches to optimise predictability of models and recombinant technology/ toxicokinetics assays to identify metabolic routes and screen mixtures of environmental health importance.

Perspective on risks posed by mixtures of chemicals

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SUMMARY

This talk aims to describe why the risk assessment of the potential toxic effects of chemical mixtures is an extremely difficult task, and to highlight industry-led recent research on testing approaches.

Determining mixture effects is a complex issue as a huge number of interactions between the various chemicals are possible. This has yet to be resolved in its entirety. It remains to establish whether mixtures of chemicals could lead to an increase in toxicity, greater than that anticipated when assessing individual chemicals in isolation. It is also possible that the components of the mixture will cancel each other out and so the overall hazard is reduced. It is useful to assess which of this attributes a specific mixture exhibits.

Partial dose and/or effect addition where different chemicals can act both on the same and on different target sites or receptors at the same time could often be the case.

Further investigations are needed in these areas and others, including low potency, biological plausibility of effects, kinetics of mixtures and overlapping mode of actions, relevance to margin exposure. This underlines the importance of a cautious research approach.

Additionally, the estimation of exposure from multiple sources is a key research opportunity. To contribute to this, the Long Range Research Initiative (LRI) Programme of the European Chemical Industry is launching a research project on “Realistic estimation of exposure to substances from multiple sources” to develop quantitative aggregate exposures methodologies.

Combined effects of natural stressors and chemicals

Chair: Dr. Jürg Oliver Straub, Co-chair: Prof. Martin Holmstrup

Integration of natural stressors in ecotoxicology: trends and future directions

Prof. Martin Holmstrup, Aarhus University, Denmark

Interactions between natural environmental factors and toxic chemicals – a metaanalysis

Prof. Ryszard Laskowski, Jagiellonian University, Poland

Effects of chemical and thermal stress on the bank vole, *Myodes glareolus*

Dr. Renata Swiergosz-Kowalewska, Jagiellonian University, Poland

Chemicals and "natural" stressors: conceptual relations and implications for assessments

Dr. Timo Assmuth, Finnish Environmental Institute, Finland

Ecological vulnerability analysis as a new conceptual technique in risk assessment

Dr. Marieke De Lange, Alterra, The Netherlands

Ecological Exposure model for assessing the risk of chemical and non-chemical stressors to terrestrial vertebrates

Dr. Mark Loos, Radboud University, The Netherlands

Introduction

Ecotoxicological risk assessment of environmental chemicals is to a large extent based on results of laboratory studies where the test organisms are exposed to a range of concentrations of single compounds. This approach is useful for the generation of dose-response relationships and derivation of indications of toxicity such as the concentration causing 50% effect on a life history trait (e.g. LC50 or EC50). In such laboratory experiments the test organisms often have optimal conditions (temperature, moisture, food etc.) to optimize performance in the control treatment and isolate the effects of the chemical in question. This is the advantage of traditional laboratory testing, and methods have been greatly improved and standardised during the last decades. However, organisms in their natural settings rarely experience optimal conditions; on the contrary they are during most of their lifetime forced to cope with sub-optimal and occasionally stressful environmental conditions, which may or may not alter the effects of a given contaminant when organisms are exposed under field conditions as compared to well-controlled laboratory conditions. Risk assessment procedures therefore often apply safety factors (or uncertainty factors) in order to make conservative estimates of environmental concentrations that do not pose any risk to species in the field. Underestimation of risk is, of course, problematic but overestimation of risk may have considerable economic consequences that are also undesirable. In order to provide a scientific basis for improving the setting of safety factors, it therefore seems appropriate to supplement traditional ecotoxicological and toxicological testing with investigations of how natural stressors interact with chemical stressors. However, even though “multiple stress” (or “cumulative stressor”) approaches have received increasing interest in the last decades such studies are still relatively scarce, and much research is needed before a comprehensive overview of this problem is available. The NoMiracle project and many other research groups have contributed to this field of research, and in this session some of this work is being presented.

Integration of natural stressors in eco-toxicology: Trends and future directions

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SUMMARY

Putting eco-toxicology into an environmental context, where the interactions with natural stressful conditions are investigated, has received sporadic interest in the early years of eco-toxicological research, but seems now to be a much more widespread topic. The NoMiracle project has advanced this research in certain areas. Test designs have been developed providing the basis for evaluations of the interactions between effects of natural and chemical stressors, and various statistical models have been applied to judge whether combinations of stressors result in effects higher or lower than expected from the single stressors. Such a framework was not available before NoMiracle. A considerable number of chemicals have been tested in combination with other stressors such as pathogens, limited oxygen, heat, cold or desiccation. Thus, NoMiracle has provided a first overview, although far from comprehensive, of which combinations of natural stressors and certain classes of chemicals may be of concern for risk assessment, and which are not. Most of these results are, however, of phenomenological character, and do not provide mechanistic explanations for interactions between effects of two different types of stressors. Such research is important and needed in order to extrapolate the results and predict the risks associated, for example, with scenarios of pollution in a changing climate.

Interactions between natural environmental factors and toxic chemicals – a meta-analysis

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SUMMARY

In this presentation we review studies on interactions between natural environmental factors and toxic chemicals, which were performed mostly under the EU 6th Framework Project "NoMiracle". We address problems arising from these interactions for ecological risk assessment. Such effects are not taken into account by standard eco-toxicological tests, even if most studies show that effects of toxic chemicals on organisms can differ vastly depending purely on environmental conditions.

We compiled data from 61 studies on effects of temperature, moisture and dissolved oxygen on toxicity of a range of chemicals representing pesticides, polycyclic aromatic hydrocarbons, plant protection products of bacterial origin and trace metals. Among the studies considered in the compilation, 51 were done on invertebrates, and 10 on vertebrates, representing both aquatic and terrestrial species. In 62.3% cases, significant interactions ($p \leq 0.05$ or less) between natural factors and chemicals were found, reaching 100% for the effect of dissolved oxygen on toxicity of waterborne chemicals. The more conservative approach to the data, assuming all analyzed cases as one study and re-calculating significance levels with the sequential Bonferroni procedure, resulted in significant interactions between chemicals and natural factors in 36.1% cases. The meta-analysis of the studies showed that the null hypothesis assuming no interactions between chemicals and natural factors should be rejected at $p=3.04\times10^{-81}$.

In a few cases of more complicated experimental designs, also second-order interactions were found, indicating that natural factors can modify interactions among chemicals. Such data emphasize the necessity of including information on climatic conditions and variation in climate across geographic regions in environmental risk assessment. However, this can be done only if appropriate eco-toxicological test designs are used, in which test organisms are exposed to toxicants at a range of environmental conditions. We advocate designing such tests for the second-tier ecological risk assessment procedures.

Effects of chemical and thermal stress on the bank vole, *Myodes glareolus*

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SUMMARY

The full factorial experiment was conducted to study combined effects of temperature and toxic chemicals (nickel - Ni and chlorpyrifos - CPF) on the bank vole. The experiment was divided into three phases: acclimatisation (3 days), intoxication (42 days) and elimination (21 days). During the intoxication animals were orally exposed to different doses of Ni (0, 300 and 900 mg/kg) or CPF (0, 50 and 350 mg/kg) or a mixture of both chemicals and different temperatures: 10, 20 or 30ºC. During acclimatisation and elimination, the bank voles were given uncontaminated food. The animals were sacrificed at 0, 5, 10, 20, 42, 49 and 55 day and the kidney, liver, brain and gonads tissue samples were obtained for chemical analysis.

The results showed that Ni absorption and accumulation in the tissues was dose dependent. Nickel was accumulated mainly during the first days of exposure (up to the 5th day), and was quickly eliminated during the elimination phase. Temperature did not have significant effect on nickel accumulation. The highest concentrations were found in the testicles, and the lowest in the liver of bank voles.

AChE activity in the brain of bank voles was significantly influenced by exposure to chlorpyrifos and was affected also by temperature during the intoxication. The lowest AChE activity was found in the brain of voles exposed to the highest CPF concentration at 10ºC. During the elimination phase the negative effects of earlier exposure to CPF as well as effects of interactions between all studied factors were still significant.
The higher induction of Mt-I gene was noticed in the kidney than in the liver tissue. Temperature was not an important factor for Mt-I induction in the tissues.
Day of exposure and temperature affected the body mass of voles. The exposure to multiple factors resulted in high mortality of bank voles.

The study was supported by the EU Integrated project NoMiracle (contract No. 003956)

Chemicals and "natural" stressors: Conceptual relations and implications for assessments

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SUMMARY

The conceptual definitions and relationships of chemicals and natural stressors are investigated to clarify their implications for assessment. Contrary to common thinking in risk assessment, specifically of hazardous chemicals, that concerns only man-made chemicals and separates them from natural stressors, most chemicals and also many high-risk chemicals are natural. 'Natural stressors',thus, include chemical and non-chemical such as physical and biological stressors (as well as socio-psychological stressors, to the extent that human societies are considered natural). The definition of naturalness is not clear-cut even for chemicals, as they include substances like metals and other elements (e.g. radionuclides) that are natural, but culturally enriched, and as many seemingly natural organic chemicals, including toxins, are influenced by humans more or less directly, even produced in (semi)natural systems, such as pharmaceuticals, functional food biologics and biological plant protection products. Boundaries between natural and non-natural chemicals and other stressors are especially blurred by converging technologies such as biotechnology, exemplified by pharmacrops (GM plants producing drugs). Risks of natural chemicals, thus, have complex relationships with synthetics, as demonstrated for mutagens/carcinogens and endocrine modulators. Their relations with non-chemical natural, artificial or semi-natural stressors are likewise complex, and the latter are often found to be, surprisingly, more important for overall risks than chemicals. However, instead of using this as a blanket argument to downplay risks from man-made chemicals, their relations in terms of risks depend on specifications of exposure, effect and control properties. For evaluative integrated assessment, the multi-dimensional continua between harmful and beneficial agents are added as key dimensions leading to new ontological and functional categories.

Ecological vulnerability analysis as new conceptual technique in risk assessment

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SUMMARY

Ecological risk assessment of environmental stressors is still in need of methods to predict effects at the ecosystem level. Current methods are largely based on toxicity threshold testing in a limited set of test species. Particularly for wildlife, toxicity data are scarce, and extrapolation from laboratory testing has limitations. Since species do not only differ in toxicological sensitivity, but also in ecological traits that determine their exposure to a contaminant and recovery after an effect, the concept of 'ecological vulnerability' may be more useful in ecological risk assessment. This approach was followed in the development of the ecological vulnerability analysis, where data on 19 ecological traits for 144 individual wildlife species were used to estimate the ecological vulnerability to six different types of soil contaminants.

Results showed that ecological vulnerability to essential metals copper and zinc was correlated with soil and sediment habitat preference. Vulnerability to bioaccumulating substances cadmium and DDT was correlated with higher positioning in the food web and with lifespan. Vulnerability to chlorpyrifos and ivermectin was determined by preference for soil habitats. Species vulnerability scores were then grouped into food chains or habitats, and statistically analyzed. This showed that the earthworm food chain was the most vulnerable. Mammals were generally more vulnerable than birds because of lower population resilience. Vulnerability in species at lower trophic levels differed between habitats, whereas vulnerability in higher trophic species was less dependent on habitats.

Our research shows that ecological traits of wildlife species can be used to estimate vulnerability of species, and this can be extrapolated to food chains and habitats. Results are ecologically meaningful, as actual wildlife species are involved, not laboratory fauna. In our opinion, it is a useful and ecologically relevant addition to existing approaches in ecological risk assessment.

Ecological exposure model for assessing the risk of chemical and non-chemical stressors to terrestrial vertebrates

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SUMMARY

Risk assessment traditionally focuses on single stressors. However, awareness is growing that exposure to single stressors is the exception rather than the rule. In practice, organisms are often exposed to multiple stressors, and not to chemicals alone, but to a combination of chemical, biological and physical agents. Governments are concerned to obtain a scientific background for legislation that is based on assessment and ranking of different types of environmental stress and ecosystem functioning. Ecology-based approaches can be introduced in ecological risk assessments to obtain an integrated overview of the meaning of site contamination and place the effects of contamination in the right perspective. Environmental characteristics such as habitat configuration and community characteristics such as predation and intra-specific interaction are important determinants in the ecological assessment of toxicants. Therefore, a new model called Eco-SpaCE, has been developed and is aimed at assessing and ranking of different types of environmental stressors and estimating the relative contribution of chemical stress to the overall stress. It focuses on the receptor, and incorporates ecological relevant parameters (food web based approach, spatial habitat variation, and predation) into exposure modelling. Such a model can help to derive options for managing, to prioritize in management options and to reduce the local risks.

New concepts and techniques in fate and exposure assessment

Chair: Prof. Gerrit Schüürmann, Co-chair: Prof. Philipp Mayer

Abraham model for K_{mw} as new surrogate for predicting bioconcentration and baseline toxicity

Prof. Gerrit Schüürmann, Helmholtz Centre for Environmental Research - UFZ, Germany

"Chemical activity" as a key parameter describing available exposure

Prof. Philipp Mayer, Aarhus University, Denmark

Passive dosing to control the exposure level of hydrophobic compounds and their mixtures

Dr. Kilian E. C. Smith, Aarhus University, Denmark

A water-sediment screening tool for measuring biodegradation of organic chemicals

Dr. Thomas Junker, ECT Oekotoxikologie GmbH, Germany

Modelled and monitored variation in space and time of PCB153 concentrations in air, sediment, soil and aquatic biota on European scale

Dr. Mara Hauck, Radboud University, The Netherlands

Development and validation of an integrated model for children's exposure to lead in Hoboken, Belgium

Dr. Arnout Standaert, VITO, Belgium

A full chain mechanistic approach assessing exposure to multi-source air pollutants and cancer risk

Dr. Spyridon Karakitsios, Joint Research Centre of the European Commission, Italy

Abraham model for K_{mw} as new surrogate for predicting bio-concentration and baseline toxicity

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SUMMARY

In the recent years, the membrane/water partition coefficient K_{mw} has become a promising alternative approach to better mimic the bio-partitioning of organic compounds in comparison to the traditionally applied octanol/water partition coefficient K_{ow}. However, the data base for the K_{mw} is extremely small. Furthermore, K_{ow} values can be predicted from chemical structure by a large number of theoretical methods, and there is no adequate model to predict membrane/water partition coefficients.

To obtain experimental values, the solid-phase microextraction (SPME) method in combination with chromatographic analysis was modified, and the obtained results were verified by comparison with values obtained experimentally using the traditional methods equilibrium dialysis and ultracentrifugation. For the modelling of the phase partitioning processes, an Abraham type LSER has been fitted to these data and additional values from literature.

This model is applied to examine the usefulness of K_{mw} to model the bio-concentration factor (BCF) and aquatic toxicity, with remark to the mode of action of the chemicals in the test set. The approach is compared to existing models, with particular attention to K_{ow} models.

"Chemical activity" as key parameter describing available exposure

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SUMMARY

The chemical activity quantifies the potential for spontaneous physico-chemical processes such as diffusion, sorption and partitioning. For instance, the chemical activity of a contaminant in sediment determines its equilibrium partitioning concentration in sediment organisms and gradients in activity determine the direction and extent of molecular diffusion between sediment and organism. Chemical activity is closely linked to both fugacity and freely dissolved concentration, which all can be measured by equilibrium sampling into thin polymer coatings. Within the NOMIRACLE project a suite of different equilibrium sampling formats have been developed, which will be presented. The advantages and limitations of chemical activity as future exposure parameter will be discussed with emphasis on baseline toxicity, toxicity cut-off phenomena and the exposure to complex mixtures.

Passive dosing to control the exposure level of hydrophobic compounds and their mixtures

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SUMMARY

Practical methods are needed to establish defined and constant exposure levels of hydrophobic organic chemicals in aquatic toxicity, bioconcentration and fate testing.This is a real methodological challenge, since these compounds are characterised by low aqueous solubilities and the propensity to sorb to various matrices. This leads to system losses and poorly defined exposure, which challenges the interpretation of observations linking for instance exposure and effect. In this regard, passive dosing as a tool for establishing and maintaining defined dissolved exposure concentrations of HOCs plays an important role. This involves the partitioning of HOCs into the test medium from a biologically inert silicone phase loaded with the chemical(s). Within the EU project OSIRIS several passive dosing formats were developed and optimized suited for experiments at size-scales ranging from millilitres to litres. Loading of the silicone with HOCs by partitioning from a methanol solution is rapid, and leads to defined and reproducible silicone concentrations. When introducing the loaded silicone into the test medium, equilibrium is fast (hours), and the highly reproducible dissolved exposure concentrations are maintained for the test duration. Passive dosing has been successfully applied to control HOC exposure to, for example, aquatic invertebrates in limit (maximum solubility) tests, dose-response type tests and for mixtures of HOCs. Applications of passive dosing for controlling exposure in dry media such as soil as well as in biodegradation studies will be discussed.

A water-sediment screening tool for measuring biodegradation of organic chemicals

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SUMMARY

Besides the experimental evaluation of the biodegradability of chemicals, the prediction of the environmental fate of compounds using theoretical models is attracting more interest in recent years. However, available models were developed mainly for organic compounds with simple molecular structures, and most of the underlying experimental data were generated in qualitative form (e.g. ready vs. not ready biodegradable). Moreover, available data sets are, typically, related to water-only systems and not to sediments, where sorption, ageing, sequestration and cross coupling may affect bioavailability, transformation and degradation. Consequently, the prediction of degradation/dissipation half-lives of chemicals in outdoor systems is hampered by the lack of quantitative, or, at least, semi-quantitative data that apply to more realistic conditions. To overcome these shortcomings, a water-sediment screening tool (WSST) was developed based on the OECD guideline 301 C (MITI I) to generate biodegradation data.

The WSST and experimental procedures were tested and validated using aniline and benzoic acid as model substances, and the results of biodegradation experiments with selected test compounds were compared with respective literature data. The results show that the WSST is well suited to determine kinetic biodegradation data required to predict the biodegradation behaviour of organic chemicals in water-sediment systems. Furthermore, the data can be used to improve quantitative structure-property relationships (QSPRs).

Modelled and monitored variation in space and time of PCB153 concentrations in air, sediment, soil and aquatic biota on a European scale

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SUMMARY

We evaluated various modelling options for estimating concentrations of PCB-153 in the environment and in biota across Europe, using a nested multimedia fate model coupled with a bioaccumulation model. The most detailed model set up estimates concentrations in air, soil, fresh water sediment and fresh water biota with spatial-explicit environmental characteristics and spatial-explicit emissions to air and water in the period 1930-2005. Model performance was evaluated with the root mean square error (RMSE), based on the difference between estimated and measured concentrations. The RMSE was 3.6 for air, 5.5-6.2 for sediment and biota, and 8.9 for soil in the most detailed model scenario. Generally, model estimations tended to underestimate observed values for all compartments, except air. The decline in observed concentrations was also slightly underestimated by the model for the period where measurements were available (1989-2002). Applying a generic model setup with averaged emissions and averaged environmental characteristics, the RMSE increased to 10 for air and 42-47 for sediment. For soil the RMSE decreased to 3.5. We found that including spatial variation in emissions was most relevant for all compartments, except soil, while including spatial variations in environmental characteristics was less influential. For improving the prediction of concentrations in sediment and aquatic biota, including emissions to water was found to be relevant as well.

Development and validation of an integrated model for children's exposure to lead in Hoboken, Belgium

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SUMMARY

Human health concerns regarding lead exposure focus mostly on children, because they, typically, have higher exposure than adults due to mouthing behaviour. Children absorb lead to a higher extent and are more susceptible to its negative effects.

The community of Hoboken (near Antwerp, Belgium) is located north-northeast of a non-ferrous plant which has been operational since the late 19th century. Blood lead levels (BLL) of children living within a 500 m distance from the plant have been followed up on a regular basis since the 1970's. Due to reduction of lead emissions and interventions at the population level, average blood lead levels dropped below 10 µg/dl in recent years. However, little is known about environmental and blood lead levels of children living in the wider surroundings of the plant.

Therefore, an environmental measurement and bio-monitoring campaign was conducted in the area situated between 500 m and 3 km from the non-ferrous plant. A reference area was included in the study. The monitoring campaign measured blood lead levels of 593 toddlers aged 2.5 to 7 years and going to school within the selected area or the reference area. Questionnaires were filled out and samples of street dust, soil, indoor dust and indoor and outdoor air were analyzed for lead and other metals.

Based on these data, an exposure model was built centred around US-EPA's IEUBK model, extending it with a wrapper model component allowing for a more accurate modelling of children's whereabouts and activities. Blood lead level predictions were validated against measured BLL from the bio-monitoring campaign, both for individual children as for pooled groups based on home location and school frequented. The relative importance of different exposure routes was investigated and the influence of home and school location was illustrated.

A full chain mechanistic approach assessing exposure to multi-source air pollutants and cancer risk

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SUMMARY

The aim of the present study is the construction of an integrated modelling environment for assessing exposure and carcinogenic risks to environmental stressors under a robust biological basis. Thus, an integrated modelling environment was compiled in a single computational platform (asclXtreme), including calculation of emissions, dispersion, exposure modelling, internal dose and cancer risk. The main component of the platform is a generic Physiology Based Toxico-Kinetic model, which can be properly modified and parameterized for the needs of individual stressors. Uncertainty and variability of the affecting parameters (in each stage of the full chain approach) were estimated through Marcov Chain Monte Carlo. The platform was parameterized to address three different environmental stressors, named as 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanone, which is responsible for lung cancer, benzene, which is known that causes leukemia and formaldehyde, which causes nasopharyngeal cancer. Although these three toxic contaminants have different main sources of origin (either indoor or outdoor), they have also a significant common indoor emission source due to ETS (environmental tobacco smoke) presence. Thus, a computational platform that takes into account the emission sources, the indoor-outdoor interaction, the exposure pattern, the internal dose and finally the carcinogenic potential provides a more realistic way for assessing health implications. Furthermore, the impact is of different policy scenarios aiming in the same health endpoint mitigation can be precisely evaluated. An example of such an application is the evaluation of different policies (traffic renewal and smoking banning) aimed at reducing leukemia risk due to benzene exposure in Greece and Finland. The results of the study indicated a different response between these two countries (leukemia risk reduction equal to 70% and 10% under traffic policy scenarios, 15 and 60% under smoking banning for Greece and Finland, respectively), attributed to the individual characteristics of traffic composition, time activity patterns and environmental conditions.

Mixture effects – description and prediction

Chair: Dr. David Spurgeon,
Co-chair: Dr. Claus Svendsen

Assessing mixture effects using a systematic biology approach

Dr. David Spurgeon, Population, Molecular and Community Ecology Centre for Ecology & Hydrology, UK

DEB approach to effects of mixtures

Dr. Jan Baas, VU, The Netherlands

Mixture toxicity studies with zebrafish (*Danio rerio*) and chironomids (*Chironomus riparius*): effects on different biological levels

Dr. Miriam Langer, University of Tübingen and LIMCO International , Germany

Systems biology assessment of binary mixture effects in the social amoeba *Dictyostelium discoideum*

Dr. Francesco Dondero, DISAV, University of Piemonte Orientale, Italy

Assessment of potential of prochloraz to enhance the effect of esfenvalerate in aquatic microcosms

M.Sc. Maj-Britt Andersen, University of Copenhagen, Denmark

Anomalous behaviour of chemical binary mixtures

Prof Miloň Tichý. National Institute of Public Health, Czech Republic

Development of a toxicological database to aid the risk assessment of exposure to mixtures of compounds

Dr. Richard Glass, Food and Environment Research Agency, UK

Assessing mixture effects using a systematic biology approach

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SUMMARY

Organisms living in the real world are simultaneously challenged by a range of stressors. Within NoMiracle new approaches have been developed to assess potential effect associated with these mixtures. One area of research into multiple stressor effects that has provided one of the greatest challenges and may reap the greatest future rewards is the development of new tools and techniques that improve the mechanistic basis for effect prediction. The starting point for this work has been an acceptance of the existing dogma that mixture effects are mostly additive (i.e. non interactive). Mode of action assessment, thus, becomes an important components of any mechanistic assessment. While often portrayed as a simple issue, in reality assessing mode of action is complicated by the fact that it is often uncertain exactly how similar the system effects of two chemical should be. While exisiting model for joint effect prediction of non-interactive mixtures do have some value, they are not panaceas: interactions between mixture components can and do occur. To address the issue of identifying interactions and understanding their causes, both statistical and mechantic approach to mixture assessment have been used. This has allowed us not only to assess how frequently interactions cause actual toxicity to deviate from prediction (and to establish the magnitude of those deviations); but also to develop methods that can be used to attribute observed deviations to interactions occuring in environmental media, during toxicokinetics or as a result of interactive toxicodynamic effects occur at the detailed mechanstic level. The relevance of these approaches for mixture toxicity has also been assessed for addressing combined effects and it is suggested that these tools and techniques can have a wide application within stress ecology.

DEB approach to effects of mixtures

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SUMMARY

A novel process-based method to assess effects of mixtures is presented. The method rest on the Dynamic Energy Budget (DEB) Theory and takes the organism as a starting point (instead of taking the effects as a starting point and linking these to concentrations). Taking the organism as a starting point has some major advantages: effects of mixtures on different endpoints at different points in time can be interpreted within one single consistent framework. Having a theoretical framework also allows for extrapolation of experimental results to other points in time, to compounds that were not measured or even to different organisms.

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Mixture toxicity studies with zebrafish (*Danio rerio*) and chironomids (*Chironomus riparius*): effects on different biological levels

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SUMMARY

In the present study, chironomids (*Chironomus riparius*) and zebrafish (*Danio rerio*), two established test organisms in eco-toxicology, have been used to examine the effects of different single substances and selected binary mixtures, such as nickel, chlorpyrifos, imidacloprid, thiacloprid, 3,4-dichloroanilin, and diazinon. By choosing these substances, we covered different modes of toxic action as well as different target sites. To obtain a holistic overview of potential effects, endpoints at different levels of biological organisation, such as stress protein (hsp70) induction, acetylcholine esterase inhibition, hatching rate, deformities, behavioural changes and survival, as well as developmental time have been studied with both test organisms. In binary mixtures of substances acting on the same target site, independent of the specific mode of action, almost all tested endpoints followed the same mixture toxicity pattern (either concentration addition (CA) or independent action (IA)). However, mixtures containing two substances with variable target sites, e.g. nickel and chlorpyrifos, showed deviations from the IA model, depending on the specific endpoint.

For zebrafish, loco-motor activity as well as the inhibition of the enzyme acetylcholine esterase, were the most sensitive endpoints for the neuro-toxic insecticide chlorpyrifos. When exposed to diazinon, acetylcholine esterase activity was inhibited already at 0.5 mg/L in developing zebrafish, whereas all other parameters responded first at 1 or 2 mg/L. The rate of deformities was the most sensitive parameter for exposure to 3,4-dichloroaniline, a degradation product of several herbicides, with effects at 0.25 mg/L compared to 0.5 mg/L for loco-motor activity and mortality.

For chironomids the survival rate as well as the total emergence rate were the most sensitive endpoints for imidacloprid (1µg/L) and thiacloprid (0.5µg/L) followed by behaviour changes. Other endpoints like deformities, developmental time, or hatching rate seemed to be unaffected by these neuro-toxic substances at sub-lethal concentrations.

Systems biology assessment of binary mixture effects in the social amoeba *Dictyostelium discoideum*

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SUMMARY

System toxicology is a research framework integrating different high throughput molecular patterns with biological and phenotypical biomarkers aimed to mechanistically describe and possibly explain the molecular adaptations to the toxic environment and the toxic effects of pollutants. Here we present a systems assessment on the effects of a binary mixture of Ni and the organophosphate biocide Clorpyrifos in the unicellular eukaryote Dictyostelium discoideum.

Both acute and chronic exposure of Dictyostelium amoebae to Nickel and the biocide Clorpyrifos resulted in a very high tolerance to the heavy metal (3h LC50>70mM; 24h LC50=6.4 mM), and high sensitivity to the organophosphate (3h LC50=17 10^-3 mM; 24h LC50=18.6 10^-3 mM). However, amoebae challenged with Chp showed a significant decrease of toxicity when Ni amounts were added to the medium. This result was observed in mortality test, sub-lethal biomarker, genotoxicity test (micronuclei frequency) and cell replication rate.

In samples exposed to the mixture for 3 h, high density microarrays showed 131 unique genes (60%). Among these, Gene Ontology annotation and a hypergeometric enrichment statistics evidenced up to 14 different oxidoreductase genes (mostly down-regulated), involved in glucose and alcohol metabolism: 4 sequences belonging to the Cyp450 like Mixed Function Oxidase super-family (3 out of 4 down-regulated), which might be involved in Chp activation/detoxification. Furthermore, the molecular fingerprint evoked by the mixture lacked those genes involved in peroxisome proliferation and gluconeogenesis, which characterized the response to the pesticide alone, as well as those involved in cell replication and DNA repair. Bi-dimensional electrophoresis data showed a protein pattern in accordance with transcriptomics data.

In conclusion, the systems assessment provided an indication that in Dictyostelium amoebae non-toxic amounts of Ni decreased Clorpyrifos toxicity at different level of biological organization (sub-cellular, cellular, organism and population). Most importantly, at the basis of the antagonistic effects of the mixture, there are both quantitative and qualitative differences in gene and protein expression profiles.

Assessment of the potential of prochloraz to enhance the effect of esfenvalerate in aquatic microcosms

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SUMMARY

The risk assessment of pesticides has traditionally been based on single compounds even though they occur as mixtures in the environment. The imidazole and triazole fungicides have, however, been shown to enhance the effect of pyrethoid insecticides. Both the fungicides and the pyrethroids are widely used and are, at times, applied to fields as tank mixtures. Hence, they may be found together in surface waters.

In this study, we assessed the toxicity of prochloraz, esfenvalerate, and a mixture of the two pesticides to zooplankton in aquatic microcosms. The microcosms (eighteen 12,000L outdoor microcosms situated at the University of Guelph, Canada) were treated once with either esfenvalerate alone at concentrations of 0.167, 0.333 or 0.833 µg esfenvalerate L^{-1}, or as a mixture with 90 µg L^{-1} prochloraz, which was also assessed singly. The zooplankton community was monitored at days -1, 1, 2, 4, 7, 14, 21 and 28 after treatment, together with pesticide concentration, chlorophyll content and physicochemical factors. Community data from the first two weeks after application will be presented. Preliminary results show that the addition of prochloraz had no effect on the zooplankton community in itself, but that it enhanced the effects of esfenvalerate severely for both cladocerans, copepods and chironomidae. Populations of cladocerans, copepods and chironomidae were knocked down at all concentrations of the pesticide mixture after four, seven and seven days, respectively, while it took two weeks to obtain a similar effect on cladocerans and chironomidae for the treatments with esfenvalerate alone. Only the highest concentration of esfenvalerate alone knocked down the copepod population after seven days. The rotifera population increased with increasing esfenvalerate concentrations both with and without prochloraz. The study concludes that the synergistic effects of prochloraz can be observed at relatively low prochloraz concentrations under field conditions.

Anomalous behaviour of chemical binary mixtures

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SUMMARY

Anomalous behaviour of effects of two chemicals in their aqueous solutions was studied using 3-min *Tubifex* and 30-min hepatocytes assay. The assays made it possible to measure acute toxic effects in mixtures of molar concentration ratios from „one pure chemical to the other pure chemical“ -0 to 1 (R-plot). Chemicals of various sources were traced: industrial chemicals and waste of industry, waste from pharmacy or agriculture. Antagonism, synergism, potentiation, inhibition and additivity were noticed in dependence on a ratio of chemicals in mixtures. In case the chemical was badly soluble, an effect of the soluble chemical on the activity of its saturated solution was measured. Highly interesting results were obtained with diclophenac and divalent cations Ni(II), Cd(II). Their R-plot indicates a total inhibition in some regions of R. If solutions measured are transparent as in *Tubifex* assay, a precipitate is noticeable which does not contribute to total acute toxicity of a mixture. Paradoxically, it means that pollutants can inhibit acute toxicity each other and, thus, contribute to an improvement of environmental health. Simultaneously, partition coefficients between n-octanol and water of the mixtures were measured. Changes were identified with the same mixtures as in the biological assays. The total partition coefficients and those of the individual chemicals changed in a various ways. The work was also supported by a grant of Ministry of Education of Czech Republic no. BB08075.

Development of a toxicological database to aid the risk assessment of exposure to mixtures of compounds

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SUMMARY

Current risk assessments tend to focus on the effect of exposure to single compounds, or compounds with a common end point. The toxicology of mixtures has become an increasingly important issue, and with respect to food safety requires that consideration is given to possible interactions between a wide range of compounds found either naturally or as contaminants in food and feed. An EFSA funded project is developing a database which will, when completed, contain details of toxicological references related to the effects of human exposure to mixtures of a wide range of naturally occurring and synthetic compounds. The database has been developed using MySQL (an open-source relational database running on Debian Linux), which is hosted on the FERA website. The application is developed using open standards as a three tier Web database model using the Web application server Adobe ColdFusion. The web pages are developed in HTML and CFML (ColdFusion Markup language). ColdFusion is primarily used to generate HTML for interactive web pages, but also allows outputting in an arbitrary, character-based format, such as XML, CSV, PDF etc., so that output files of references are compatible with EndNote. Access to the website is secured using encrypted passwords and the SSL protocol. This will ensure that all data updates are secure and will enable appropriate access control for individual users. Literature searches are being done to populate the database with relevant reports which are being reviewed by international experts, initially within FERA, based on the Cochrane Collaboration. As the literature searches are completed the database will become a key tool which will allow the user to search for reported toxic effects of particular compounds of interest, such as pesticides, botanicals, mycotoxins, etc. when present in mixture with other compounds.

Risk of mixed exposures to metals

Chair: Prof. Staffan Skerfving,
Co-chair: Prof. Alfred Bernard

Public health impact of long-term, low-level mixed elements exposure in susceptible population strata – results from the EU project PHIME

Prof. Staffan Skerfving, PHIME Coordinator, Lund University, Sweden

Mechanisms to cope with cadmium excess in plants

Prof. Michael Gjedde Palmgren, University of Copenhagen, Denmark

Exposure to metals from ferroalloy plants: preliminary results of exposure assessment and neurofunctional survey in Italian adolescents

Prof. Silvia Zoni, University of Brescia, Italy

Mixed exposure to metals and oxidative DNA damage, influence of gene-metal interactions – report from ongoing projects

Dr. Karin Broberg, Lund University, Sweden

Mercury as a risk factor for myocardial infarction and stroke: the Northern Sweden Study

M.Sc. Maria Wennberg, Umeå University, Sweden

Impact of lead, cadmium and inorganic mercury on the health of adolescents: a biomarkers study in Belgium

Prof. Alfred Bernard, Catholic University of Louvain, Belgium

Introduction

This session is dedicated presentations from the PHIME Project (Public Health Impact of long-term, low-level Mixed Element exposure in susceptible population strata). The project contains a long series of multiple stressor aspects. Several of these are discussed in the session.

Humans are exposed to a mixture of toxic elements. Several of those affect the same target organs. Hence, one of the main objectives of PHIME is to study effects of mixed exposures. Important examples are the combined toxicity on the developing central nervous system (CNS) by methylmercury, arsenic, manganese, lead and cadmium. Epidemiological studies are performed in the Faroe Islands, Seychelles, Mediterranean area and Bangladesh. Further, several toxic elements (cadmium, mercury and lead) accumulate in the same part of the kidney. Thus, it is possible that there is a summary effect on kidney function. Such interaction is the subject of studies in Belgium and Bangladesh, and in biobanked samples from Swedish uremia cases.

Despite centuries of toxicological studies, the critical mechanisms of several elements are still not clear. It is generally assumed that oxidative stress is important (lead, cadmium, mercury, arsenic, manganese). PHIME addresses possibility of common mechanistic pathways in studies of biomarkers of oxidative stress, as well as the potential of a gene-environment interaction as regards polymorphisms in genes for enzymes involved in the protection against harmful effects of oxidative stress. Such phenomena may explain the well-known inter-individual variation in susceptibility to toxicity of metals, as well as between populations with varying genetic background. Such effect modification has a great importance for risk assessment of toxic elements.

But the elements may also interact with other toxic agents affecting the same target. An important category of environmental pollutants is the persistent organohalogen ones (POPs). They are well known to affect the developing CNS. Hence, PHIME studies address potential interaction. Also, POPs are known to affect the skeleton. Since cadmium is a potent inducer of bone effects, it is natural for PHIME to address the possibility of a summary effect in subjects exposed to both pollutants. Another type of contaminant with potential to interact with elements is the mycotoxin ochratoxin A, which is a major problem in grain from several geographical areas. Since it affects the same renal proximal tubuli as cadmium, lead and mercury, PHIME investigates the potential of interaction in a study in Marocco.

It is likely that the nutritional status modifies the toxicity of metals. But the important "nutritox" area has been studied only occasionally. Thus, several PHIME investigations address such aspects. For example, the potential of an effect modification by nutrients of the toxicity of metals on the developing brain, such as a positive effect of long chain n-3 polyunsaturated fatty acids and selenium, are important aspects in work-packages dealing with methylmercury, arsenic and manganese. Also, there is a potential of an interaction of these nutrients with a toxicity of methylmercury on the cardio- and cerebrovascular system.

Further, both toxic and essential elements accumulate in plants. However, the mechanisms behind the turnover are still not sufficiently known, and thus not possibilities to simultaneously increase essential

and decrease toxic elements, into patterns beneficial for health. One of the pillars in PHIME is devoted to these aspects.

Of course, risk-benefit considerations are important issues in most PHIME activities.

Public health impact of long-term, low-level mixed elements exposure in susceptible population strata – results from the EU project PHIME

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SUMMARY

The overall aim of PHIME is to improve the integrated health risk-assessment of environmental exposure to toxic and essential metals via food, addressing the complexity of exposures, interactions, risk groups (including women, children, the elderly and individuals with genetic susceptibility), nutrition, and mechanisms of action. Moreover, the understanding of mechanisms for uptake of metals in plants and, thus, into the human food chains, will be increased. This will enable preventive measures to be taken in order to reduce the metal burdens and their health consequences.

Major steps have been taken as regards all three main objectives: I. What are the problems? II. Where are the problems? III. Possible solutions to the problems (some).

The general population has a mixed exposure to metals. A PHIME study of lead, cadmium (Cd) and mercury (Hg) in blood in children from nine countries has displayed wide variations in exposure. Seafood is the major source of exposure to methylmercury (MeHg). An important part of the MeHg problem is the effect on the brain of the foetus and infant, which is studied in the Faroe Islands, Seychelles and Mediterranean. The results display important interaction with long-chain n-3 polyunsaturated fatty acids. Hg may also affect the cerebro- and cardiovascular systems, which is addressed in studies in Finland, Sweden and the Faro Islands. Again "nutritox" interactions are in focus. Both Cd and persistent organic pollutants (DDT, PCB) are toxic for the skeleton. However, at the exposures in Sweden, there was no interaction.

Mechanisms to cope with cadmium excess in plants

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SUMMARY

Crops, such as wheat, absorb cadmium (Cd) efficiently from soils containing even very low concentrations of Cd derived from the bedrock, mineral fertilizers or applications of sewage sludge. Plants have a moderate tolerance for Cd and can accumulate Cd to levels above the concentrations considered to be safe in human food without developing visible toxicity symptoms. As cadmium is highly toxic for humans at low concentrations and is a known carcinogen, intake via apparently healthy plants is an increasing concern.

Previously, it was believed that toxic metals in the soil solution diffuse into plant roots and reach the shoot passively together with water. We now know that specialized membrane-bound transport proteins situated at different control checkpoints in the plant body mediate the transport of minerals. In plants, Cd is accumulated because it hitchhikes on a number of membrane transporters of iron, calcium and zinc (Zn). A key bottleneck determining the uptake of Zn and other nutrients is their active loading into the xylem, a vascular tissue securing transport of water and nutrients from the root to the shoot.

Two metal pumps (HMA2 and HMA4) in the P-type ATPase superfamily are responsible for the loading of both Zn and Cd into the xylem of the model plant *Arabidopsis thaliana*. Inactivating metal pumps in crop plants corresponding to HMA2 and HMA4 would potentially reduce accumulation of Cd in the shoot, but this approach is not likely to be feasible, as the resulting plants would suffer from shoot Zn deficiency. It is, thus, desirable to identify mutants of HMA2 or HMA4, which encode a pump that can still transport Zn at high rates but cannot transport Cd. Methods employed to optimize the metal ion specificity of HMA2 and HMA4 include site-directed mutagenesis in vitro and random mutagenesis *in vivo*.

Exposure to metals from ferroalloy plants: preliminary results of exposure assessment and neurofunctional survey in Italian adolescents

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SUMMARY

Background and Objective: Increased parkinsonism was observed in Valcamonica, a valley in the province of Brescia, Italy. Prevalence data were higher in the vicinities of ferroalloy plants and associated to the concentration of manganese in deposited dust. The aim of the present study was to assess motor, cognitive and neuro-sensory functions in adolescents in the exposed area and in a reference area.

Methods: Metals were measured in airborne particles collected with 24-hour personal samplers, and in salad sampled in local gardens. Samples were analyzed with Total Reflection X-Ray Fluorescence. Soil was analyzed at surface and 10cm depth. Adolescents were recruited through the local school system for neurobehavioral examination and assessment of dietary intake of metals. Blood and urine samples were collected for metal analysis.

Results: A total of 303 children residing in an exposed area and a reference area participated in the study. Preliminary data show airborne manganese levels of 57.78±71.33 (range 1.24-516.70) ng/m^3 in the exposed area and 13.80±11.36 (range 5.30-36.59) ng/m^3 in the reference area. Lead, iron, zinc and chromium also showed significantly higher levels. Manganese results were significantly higher also at the surface and at 10 cm depth of soil and in salad. Children in the exposed area showed impairment of motor coordination and odour identification associated with airborne manganese at multivariate analysis. Blood lead was inversely associated with IQ.

Conclusion: Environmental exposure to manganese in adolescents is related to deficit in motor and olfactory functions whereas concomitant lead exposure is related to decrease of IQ.

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Mixed exposure to metals and oxidative DNA damage – influence of gene-metal interactions – report from ongoing projects

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SUMMARY

Background:

Exposure to arsenic, cadmium, and lead may generate oxidative stress, which can be assessed by 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) in urine, a sensitive marker of oxidative DNA damage. There are inter-individual differences in toxicity of the metals, probably partly due to different genetic profiles.

Objectives:

To evaluate oxidative DNA damage induced by mixed chronic exposure to arsenic, cadmium, and lead, as well as nutritional status and genetic variation.

Material and methods:

Two populations were analysed: 1) women in Matlab, rural Bangladesh (N=220); 2) women in the Andes mountains in Argentina (only for arsenic; N=114). Cadmium, lead, and manganese were analyzed in urine and erythrocytes, while selenium and zinc in erythrocytes, all by ICPMS. Arsenic and its metabolites were analyzed in urine by HPLC-ICPMS. 8-oxodG was measured in urine using LC-MS/MS, ferritin in plasma by radioimmunoassay. Genotyping of genes for metal metabolism and defence was performed by mass spectrometry (Sequenom).

Results:

In Bangladesh, 8-oxodG was positively associated with cadmium in urine ($p<0.001$), arsenic ($p=0.001$), and fraction of the monomethylated arsenic metabolite ($p=0.004$). Manganese was negatively associated with 8-oxodG ($p=0.027$), while ferritin in plasma positively associated ($p<0.001$). In Argentina, 8oxodG was positively associated with fraction of the monomethylated arsenic metabolite ($p=0.013$). There were gene-metal interactions for genes involved in metal metabolism and DNA repair.

Discussion:

The strong positive association between cadmium and urine and 8-oxodG suggests specific mechanisms for cadmium-induced oxidative DNA damage. The influence of arsenic exposure on 8oxodG concentrations was verified in the two populations. It was not clear whether there was an additive or multiplikative effect of metal exposures on 8oxodG concentrations. Gene-metal interactions explain part of the interindividual variation observed and are important for proper risk assessment for DNA damage.

Mercury as a risk factor for myocardial infarction and stroke: The northern Sweden Study

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SUMMARY

Introduction: A beneficial role of fish intake on risk of cardiovascular disease has been reported, mostly ascribed to n-3 fatty acids. Fish is also a source of methylmercury (MeHg). Associations between elevated risk of myocardial infarction (MI) and mercury levels in hair and nails have been found in epidemiological studies.

Aim: Our aim was to elucidate whether fish intake and mercury levels in erythrocytes (Ery-Hg) is a risk factor for a first MI or stroke, and whether long-chain n-3 fatty acids in plasma (P-EPA+DHA) and selenium in erythrocytes (Ery-Se; MI only), have protective effects.

Materials and method: Within population-based cohorts from Northern Sweden, 369 cases of stroke and 738 individually matched controls were included. In a study on MI risk, 500 cases of MI and 625 controls were included.

Results: Median Ery-Hgs were 3.63 ng/g and 3.54 ng/g for the stroke and MI studies respectively. No associations were seen between Ery-Hg or P-EPA+DHA and stroke risk. Men with high fish intake had an increased risk of stroke, but in women there was a non-significant decrease of risk with increasing fish intake. In the study on MI, there was no obvious effect of reported fish intake or Ery-Se, whereas a protective effect was found with higher levels of Ery-Hg or P-EPA+DHA.

Conclusion: There is no association between Ery-Hg and stroke risk at these low levels, neither any protective effect for P-EPA+DHA. A protective effect of Ery-Hg on MI risk is found in this low exposed population, probably due to Ery-Hg being a marker for fish consumption. As for reported fish intake there is no effect on MI risk, but for stroke risk there is a sex difference, with increased risk in men and decreased in women.

Impact of lead, cadmium and inorganic mercury on the health of adolescents: a biomarkers study in Belgium

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SUMMARY

Introduction

Heavy metals polluting the environment can cause adverse effects on vulnerable populations such as children, but it is uncertain whether these metals still pose health risks at the very low environmental exposure levels now prevailing in Europe.

Objective

We studied the effects of cadmium, lead and mercury on the kidney, lung, reproductive, and immune systems of adolescents during a cross-sectional survey in Belgium.

Method

We examined 743 adolescents (412 girls, mean age, 15.5 years) who were recruited in three secondary schools in the southern part of Belgium. Children provided samples for the determination of a wide variety of biomarkers: in whole blood, lead and cadmium; in urine, creatinine, cadmium (Cd), lead (Pb), mercury (Hg), albumin and retinol-binding protein (RBP); in serum, creatinine, Clara cell protein, surfactant protein D, testosterone, inhibin B, LH, FSH, prolactin, total and aeroallergen-specific IgE.

Results

The median (interquartile range) concentrations of metals were in blood (µg/l): Pb, 15.2 (11.7-19.1), Cd, 0.18 µg/l (0.14-0.28) and in urine (µg/g creatinine): Cd, 0.093 (0.069-0.13), Hg, 0.54 (0.35-0.87) and Pb, 0.84 (0.62-1.16). The concentration of Pb in blood correlated very significantly with total serum IgE level ($p<0.001$). The concentrations of Cd and Pb in urine (but not in blood) were inversely related to serum creatinine ($p<0.001$). The concentration of Cd in urine (but not in blood) correlated with urinary RBP ($p=0.002$), but showed no associations with Hg or Pb in urine or blood. There was, however, no increase in the odds for urinary RBP >90th percentile with increasing urinary Cd ($p=0.35$). Subjects with increased urinary RBP had similar levels of urinary Cd as the rest of the population. All these associations should, thus, be interpreted with caution, especially as the association between RBP and Cd in urine appears to be distorted by some co-excretion mechanisms involving namely albumin. We found no significant associations between the biologic levels of the three metals and serum biomarkers of the lung or of the reproductive system.

Conclusion

At very low environmental exposures, significant associations still emerge between indicators of exposure to lead and cadmium and some effect biomarkers, in particular for the kidney. The health significance of these associations is currently under investigation.
This work was supported by the European Union (Phime project).

Mixture effects – patterns and trends

Chair: Prof. David Spurgeon,
Co-chair: Dr. Dorota Jarosinska

Deviations from the reference models and the possibility of predicting higher level mixture effects from binary mixture toxicity results

Dr. Claus Svendsen, NERC (CEH), UK

Assessing ecotoxicological risk for pesticide mixtures in aquatic and terrestrial ecosystems

Dr. Claudia Vaj, University of Milano Bicocca, Italy

Mixtures of hormetic compounds: what do you get?

Dr. Nina Cedergreen, University of Copenhagen, Denmark

Critical aspects and future perspective in assessing ecotoxicological risk for aquatic and terrestrial communities

Dr. Serenella Sala, University of Bicocca, Italy

Deviations from the reference models and the possibility of predicting higher level mixture effects from binary mixture toxicity results

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SUMMARY

Mixture toxicity studies are often either binary mixtures aiming to describe the entire binary dose-response surfaces, or mixtures of multiple chemicals targeting defined mixture-ratios. For mixtures with >10 components concentration addition (CA) and independent action (IA) predictions have often proved to closely reflect the observed effects. However, a recent review has found that deviations are likely to occur when a few components dominate a multi component mixture. In this presentation we will look at the overall results from the data base built from all the NoMiracle binary and ternary studies and see how they fit this general pattern. We will then also look at the potential to scale up from detailed information on binary mixtures to what may happen in mixtures of more chemicals. We have developed a model to predict the joint effect of ternary mixtures at all dose-levels and mixture ratios, based on binary mixture deviations from the reference model CA. The model is tested on 14 datasets from experiments covering the full dose-response space of both single compounds, binary and ternary mixtures, and showing both significant synergistic and antagonistic interactions. The results showed that the maximal ternary deviations from the reference model CA, could be captured by considering combinations of the deviations observed in the binary mixtures.

Assessing eco-toxicological risk for pesticide mixtures in aquatic and terrestrial ecosystems

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SUMMARY

Agro-ecosystems are exposed to complex mixtures deriving from agricultural practices: often different active ingredients are present in the formulation of a plant protection product; several PPP are applied to the same crop; several crops are usually present in intensive agricultural areas.

At the end of the productive season, a huge number of chemicals with different chemical and toxicological characteristics (herbicides, insecticides, fungicides) are released and are virtually present in the environment.

The composition of mixtures is extremely variable in space (due to land use, environmental fate of active ingredients, etc.) and in time (due to application patterns, persistence, etc.). Moreover, exposure patterns are completely different for aquatic and terrestrial ecosystems, due to different environmental fate of chemicals, as well as to different characteristics and behaviour of the biological communities.

Specific procedures have been developed for assessing eco-toxicological risk for pesticide mixtures, specifically focused to aquatic as well as to terrestrial ecosystems.

These procedures allow assessing the spatial distribution on the territory, with the possibility of producing GIS-based maps of eco-toxicological risk. Moreover, the variability in time can also be described, allowing to calculate a time trend of risk during the annual cycle.

The procedures will be compared highlighting major differences between aquatic and terrestrial (hypogean and epigean) ecosystems.

Examples of application in experimental areas will be described.

Value and limitation of the approach are also discussed.

Mixtures of hormetic compounds: What do you get?

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SUMMARY

Some chemicals give biphasic dose-response curves in certain tests. These curves are characterised by an initial increase in the response compared to the control followed by a response decrease at higher concentrations. The phenomenon is often called “hormesis”. The term can be misleading as it insinuates a common mechanism behind the biphasic dose-response relationships. Taking a closer look at different biphasic dose-response curves shows that this is rarely the case. But what happens to the size and concentration range of the response increase, when different hormetic compounds are mixed? And when hormetic and non-hormetic compounds are mixed? Can we predict the mixture effects? Examples from three test systems, a *Lemna* growth inhibition test, a lettuce root elongation test and a hormone producing cell assay will be presented. The examples show both mixtures of hormetic and non-hormetic chemicals. The results emphasise the importance of knowing the physiological mechanism behind the hormetic response, if we are to be able to predict mixture effects of biphasic dose-response curves.

Critical aspects and future perspective in assessing eco-toxicological risk for aquatic and terrestrial communities

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SUMMARY

In agro-ecosystems, natural communities are affected by several potential stress factors. Among them, the wide spread use of pesticides is one of the most relevant. Assessing and managing pesticide risk is a key issue for sustainable agriculture. The potential exposure to pesticides in aquatic and terrestrial ecosystems is a function of application patterns and of environmental fate of active ingredients. Moreover, in terrestrial ecosystems, the behaviour of non target organism plays a relevant role. Site-specific approaches are strongly recommended to refine risk assessment by applying GIS-based methodologies. The present work describes the development of site-specific methodologies and some examples of their application, highlighting critical aspects and future perspective in assessing eco-toxicological risk for non target communities (aquatic, terrestrial epygean and hypogean).

The procedures allow comparing eco-toxicological risk of active ingredients and its variability in space and time as a function of chemical properties and environmental characteristics. The application of this methodology, and its further implementations (e.g. with meteo-climatic provisional scenarios, with temporal evolution of stressors, with socio-economic assessment), could represent a tool to combine and optimise provisional risk assessment for terrestrial biodiversity in intensive agricultural areas.

Integrated risk concepts and governance

Chair: Prof. Mikael Hildén, Co-chair: Dr. Ad Ragas

Escaping risk wars and prisons: reflexive integrated assessment of stressors, causes and consequences accounting for interventions

Dr. Timo Assmuth, Finnish Environmental Institute, Finland

Developing a framework for research on individual-level Medical Risk Management

Dr. Laurel C. Austin, Copenhagen Business School and University of Copenhagen, Denmark

Communication of Chemical Risks

Dr. Christina Benighaus, DIALOGIC, Germany

Integrated risk assessment and governance in REACH

Dr. Ad Ragas, Finnish Environment Institute, Finland

Prof. Mikael Hildén, Finnish Environment Institute, Finiland

Escaping risk wars and prisons: Reflexive integrated assessment of stressors, causes and consequences accounting for interventions

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SUMMARY

I propose a concept of integrated risk assessment that extends established combinations of stressor- and effects-based approaches (e.g. linked exposure and epidemiological analysis) by fuller, more flexible and reflexive consideration of the multi-dimensionality and sequences of risk formation and of knowledge and valuation needs for interventions. The concept draws on multi-factorial causation models in etiology and multi-criteria decision analysis but amends these by integrating and iterating cascades of causes and consequences (also 'root' causes and social impacts); variation and specifics of exposed populations; the potential of low-regret risk reduction; and by considering the types and levels of uncertainty. I illustrate the approach with disease burden estimation and attribution (by the WHO methodology) and with human health risks and benefits of fatty fish. I emphasize the sensitivity of risk estimates and characterizations to framings of causes and impacts, to assumptions of their interactions, to aggregation of and weightings on (age) groups and outcomes (e.g. in Disability-Adjusted Life Years), and to consequences of interventions. I show that with multiple and cumulative stressors and outcomes, 'deep' value-laden uncertainties about risks and management gain importance, and that broad and reflexive deliberation and transparency are keys to resolving controversies about risks and benefits, and to escaping dilemmas between breadth vs. detail and paralysis by analysis vs. clueless panic action. I conclude that from a preoccupation with exact, formal, narrow and linear treatment of complex realities, risk assessments should move to better consider, and facilitate discourse on, choices and their grounds, while heuristically utilizing uncertainties, ambiguities and disputes about them to construct the relevant contextualized and experiential knowledge.

Developing a Framework for Research on Individual-level Medical Risk Management

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SUMMARY

I develop a framework for the study of individual-level medical risk management. Such a framework is needed because increasingly, seemingly healthy people face medical decisions that involve managing the risk of possible, but uncertain, future health states. Such decisions might involve cancer screening, genetic testing, vaccination, and other risk-reducing interventions. This framework builds on a normative taxonomy of five medical decision making situations, four of which involve managing risks in asymptomatic people.

When managing medical risks for symptomatic people, the process involves clinical assessment to determine the probability of a current health state, evaluating interventions' possible benefits and costs, and receiving feedback fairly quickly (i.e., the person improves, worsens, or stays the same). When managing medical risks for asymptomatic people, the process involves estimating the probability of a future health state, assessing interventions' possible benefits and costs, and receiving feedback in the long term, at the population level. For example, it is only over time, at the population level, that we can judge the effectiveness of a vaccination program. Finally, different sources of uncertainty come into play for different types of medical risk-management decisions.

The events associated with risk-reducing interventions can themselves be of great magnitude, such as preventive surgery (e.g., mastectomy), chemotherapy, or pregnancy termination. If we define risk as having two dimensions - uncertainty and severity (see Aven and Renn, 2009) – then presumably risk-management strategy preferences depend on perceptions of both dimensions. Further, medical decisions are often shared by an individual and a medical professional, and so the risk perceptions of both are relevant.

In building this framework I consider the factors discussed here, as well as others from the literature, such as emotion, dread, and framing effects.

Communication of Chemical Risks

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SUMMARY

The fast development of the chemical industry during the last hundred years has caused increasing requirements by the public, customers and politicians concerning the production, use, and disposal of chemicals. Public authorities reacted by tightening the regulation, lately with the REACH regulations enacted in 2007 by the EU. In addition to these legal requirements, more and more stakeholders request improved and comprehensive practices of risk communication. This is accentuated under REACH, which has greatly increased responsibilities of industry, including down-stream users, also in assessment. But risk communication is a challenging task. Ideally it should assist stakeholders to come to balanced judgements that reflect the factual evidence about multiple risk factors in relation to their own interests and values. Much of what we know about risk perception and communication of chemicals and cumulative stressors is known from analyses of risk behaviour. Chemicals, food additives and pharmaceuticals are often seen as artificial and, therefore, threatening to human health and the environment. This can lead people to believe that toxicity depends less on the dose than on the characteristics of the substance, especially for those substances that have reached the headlines.

Risk communication needs an integrated approach to support complex instruments for the regulation and management such as REACH. This presentation examines why it is so important to communicate risks and explore special features in the chemical risk area, specifically regarding integrated assessment and governance of cumulative risks from multiple stressors. The objectives and the risk communication concepts will be elucidated and the role of communication, perception, audience will be analysed. This provides an understanding of the different levels of risk debates and how they apply to chemicals and related stressors.

Integrated risk assessment and governance in REACH

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SUMMARY

The REACH legislation of the EU on Registration, Evaluation and Authorization of Chemicals presents, among many other things, an important case of risk management also in connection to the development of methods for addressing risks from multiple stressors. We studied the links of REACH with the assessment and management of such risks from an information and communication perspective. Based on a broad Internet survey of expert and stakeholder opinions of integrated risk assessment and risk management, we interviewed top regulators and stakeholder representatives at the EU level on integrated risk assessment generally and specifically in connection with REACH. We further arranged discussions with ECHA staff on the links between REACH and integrated risk assessment in more concrete terms, focusing on the generation and use of new information in the process. This empirical work was complemented by literature reviews and document studies of REACH as a representation of risk governance in the socio-political field, based partly on published REACH guidance. Here we present some key results and tentative insights, including questions for deliberation and further study. We first discuss concepts and interpretations of integrated risk assessment and multiple stressors that are relevant in this connection, as identified by and explored together with study subjects. We find some elements of integrated risk assessment and management under REACH, not all well-known, and new ones developing also by interaction with other fields and based on multi-actor communication. However, there are also marked barriers for the development and uptake of methods for the assessment and management of multiple stressors under this system, as it is basically focused on single chemicals and specific mixtures in products. The use of the incoming information e.g. from testing nevertheless provides opportunities also for iteratively steering the generation of information more efficiently. Further important dimensions of integration can be discerned, enriching scientific approaches to cumulative effects and risks of multiple stressors, such as the integration of exposure and effect information for developing exposure reduction options. We highlight the tension between simplification and stability of procedures on the one hand and specificity and flexibility on the other. The relation between evidence-based and precautionary assessment and management further complicate the balancing act especially in the case of complex and uncertain multi-stressor risks. We emphasize how this will require continuous and improved multi-level communication between the scientific and applied communities not only in the REACH and chemicals field but in others such as health and safety. This will also help break out the (single) chemical fixation inherent in REACH while retaining and utilizing its virtues.

New concepts and techniques for risk assessment

Chair: Dr. Ad Ragas, Co-chair: Prof. Mikael Hildén

Probabilistic ecotoxicological assessment factors

Dr. Mijke van Oorschot, Radboud University, The Netherlands

Soil quality and ecosystem services

Dr. Jack Faber, Alterra, The Netherlands

The critical issue of finding worst-case

Dr. Peter Borgen Sørensen, Aarhus University, Denmark

Can uncertainty analysis be harmonised within the FP6 funded IP projects when dealing with health impact assessments?

Dr. Alexandre Zenié, Joint Research Centre of the European Commission, Italy

Toxicity profiling: an effect-based integrative tool for water quality assessment

Dr. Timo Hamers, VU University, The Netherlands

Probabilistic eco-toxicological assessment factors

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SUMMARY

Eco-toxicological assessment factors are currently used to derive a predicted no effect concentration (PNEC) for ecosystems based on a small dataset of No Observed Effect Concentrations (NOECs) originating from single-species tests. The disadvantage of these deterministic factors is that they are not grounded by scientific research, leading to mostly conservative standards without an indication of the uncertainty level involved. Furthermore, because the lowest available NOEC or L(E)C_{50} is divided by the assessment factor, more testing often leads to stricter standards which frustrates additional testing.

The goal of our project was to develop a method to derive new probabilistic assessment factors for ecological risk assessment. A database of chronic and acute aquatic toxicity data for different species and substances was compiled. Monte Carlo simulations were used to sample lowest and geometric mean values for scenarios with different data availability, taxonomic groups and substances with various toxico-dynamic effects. In order to derive new probabilistic assessment factors, the generated values were compared to the HC_5 of the SSD or (if available) the NOEC from mesocosm studies.

The preliminary results show that the newly derived assessment factors are less conservative than the old ones and decrease with increasing sample size, which is contrary to the old method.

This method can be translated into a useful tool for policy makers for deriving more realistic standards and allows a case by case specification of the desired confidence level.

Soil quality and ecosystem services

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SUMMARY

Healthy soils provide fertility, regulate water and organic matter, prevent erosion, suppress disease, and support constructions and infrastructures. The use of soils can only be cost-effective, and land use aims can only successfully be achieved if these ecosystem services are provided. In this paper, ecological risk assessment is approached by a focus on soil ecosystem services. Depending on the type of land use, ecological requirements are derived from relevant ecosystem services. These requirements represent aspects of the soil ecosystem that are crucial to establish the ecosystem service. Examples of ecological requirements are decomposition processes or soil structuring processes. Such requirements to soil functioning can be broken down into a set of indicators that are quantifiable parameters for soil ecosystem processes or structures. Well-chosen indicators may be used to assess the impact of any stressor on ecosystem functioning and, hence, ecosystem services. By way of example, in this paper we address soil contamination. Toxicity data were compiled from the literature to assess the effect of various chemicals on indicators representing soil ecosystem services of grassland under agricultural, natural and municipal use.

The critical issue of finding worst-case

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SUMMARY

The natural evolution of stakeholders awareness, and the scientific discovery related to the human and environmental health is setting up more and more complex demands on the risk assessment methodology. Meanwhile, the available scientific knowledge and information is both increasing but also becoming more scattered across multiple scientific disciplines at the same time. Hence, the potential risky situations are becoming more multifaceted, which again challenges the risk assessor in terms of giving the right relative priority to the multitude of risk contributing factors. The only way to handle this problem is by focussing worst-case risk conditions and this presentation describes a conceptual modelling approach that selects most likely worst-case conditions based on existing knowledge, as preceding steps of a final and quantitative risk assessment. The system model can optimized and guide planning of risk assessment activities based on an initial screening level analysis and mapping of available knowledge related to the risk problem. Conventional uncertainty assessment is made primary in relation to parameters value uncertainty for the final risk assessment models, however, this is far from being a complete in relation to the purpose of risk assessment to document protection. This presentation includes uncertainty in both context and concept using knowledge mapping principles that can facilitate a more complete uncertainty assessment.

Can uncertainty analysis be harmonized within the FP6 funded IP projects when dealing with health impact assessments?

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SUMMARY

The HEIMTSA project is committed to assessing uncertainty throughout the full chain of the health impact assessment (HIA) process. Two principle probabilistic methods, Monte Carlo simulation and Bayesian analysis, are utilised within the tiered approach recommended by the WHO IPCS for uncertainty characterisation and communication in exposure assessment. This has been augmented by particular consideration of uncertainty when considering pair-wise comparisons, *e.g.* between projected scenarios and baselines. These methods have been applied to a number of case studies within the HEIMTSA project. Considering the full chain can lead to a number of issues, including the integration of different systems and dependence between parameters, which can restrict the choice of which levels of tiered approach may be used.

This presentation has three main objectives: **(i)** to illustrate the implementation of the methods within the case studies; **(ii)** to describe the harmonisation of the methodology with other two FP6 funded IP projects: INTARESE and 2-FUN and **(iii)** to discuss the possibility of integration with NoMiracle, in terms of both characterising and communicating/visualising uncertainties, which could help lead to critical mass in the use of such methods.

Although the choice of methods for characterization and visualisation of uncertainty may differ according to the particular setting, there is an underlying common approach within the three aforementioned IP projects, following the principles recommended by the WHO IPCS. Furthermore, a common IT repository for uncertainty analysis has been developed by the JRC throughout these IP projects which will allow harmonisation of terminology and the sharing of expertise and experience. This will help in facilitating the education of key users, such risk managers. The IT repository will be available for these key users, however, there will still be a requirement for an interface between this environment and the expert systems that are used in performing the uncertainty analysis.

Toxicity profiling: an effect-based integrative tool for water quality assessment

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SUMMARY

A toxicity profile is a toxicological fingerprint of the complex mixture of contaminants present in the environment. For each environmental sample, a toxicity profile can be obtained by testing its integrated potency to cause a response in a battery of bioassays each representing a different mode of action. We explored the applicability of in vitro toxicity profiles for effect-based water quality assessment using a dataset in which sediment extracts from 15 different locations in the Rhine-Meuse estuary were tested in five different bioassays. Toxicity profiles were translated into hazard profiles, indicating for each mode of action the relative distance to the desired or acceptable water quality status. Using hierarchical clustering techniques, location-specific hazard profiles of four out of five harbor locations in the test set were classified together into a cluster of harbor locations. Apparently, the fifth harbor location could be identified as a harbor with a hazard profile deviating from “normal” harbor profiles. This deviation could be attributed to relatively high dioxin-like and estrogenic potencies and may be a reason to focus on this particular location for “in depth” research into the identity and possibly the source of the responsible contaminants. Toxicity profiling and subsequent hazard profiling seems to be a tool that is directly applicable for water quality assessment. However, it requires a very careful selection of a reference toxicity profile that is either measured at a reference location or is designated as a desirable or acceptable toxicity profile for that particular location.

Risk presentation and visualisation

Chair: Dr. Peter van den Hazel, Co-chair: Dr. Joost Lahr

Maps as tools to visualise cumulative risks of pollutants

Dr. Joost Lahr, Alterra, The Netherlands

GIS-based decision support systems for spatial-oriented assessment and communication of ecological and human health risks

Dr. Andrea Critto, University Ca' Foscari of Venice, Italy

Geographically based indicator for pesticide risk

Dr. Christian Kjær, Aarhus University, Denmark

A cumulative assessment of pesticides in Europe

Dr. Alberto Pistocchi, Joint Research Centre of the European Commission, Italy

Risks in Urbania: A showcase for novel methods to assess cumulative risk

M.Sc. Louise Preeker, Radboud University, The Netherlands

Maps as tools to visualise cumulative risks of pollutants

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SUMMARY

Geographical risk maps provide a powerful tool for visualisation of the spatial distribution of environmental stressors and their effects on human health and ecosystems. There are many different types of such maps. One important distinction is the one between maps that simply show the geographical distribution of stressors and 'true' risk maps that also show the consequences. One may also map the vulnerability of areas to pollution, i.e., before pollution actually occurs. Traditionally, risk and vulnerability maps display the information for single stressors or pollutants, whereas in the real world people, animals and plants are exposed to a multitude of polluting substances and stressors at the same time. During the NoMiracle project in the past five years, novel methods have been developed for cumulative risk assessment and also for the mapping of cumulative effects of environmental contaminants, both in the area of human health risk assessment and ecological risk assessment. Examples of these maps, both from the project and from other sources, will be shown along with information on how they were made and how they can be used. One very important objective of risk maps is often to communicate the results of environmental risk assessment to stakeholders and to the general audience. However, this should be done both with great care and in a scientifically sound manner. For example, suggestive use of symbols and colours needs to be avoided. Proper risk mapping, therefore, requires a certain level of expertise in risk communication as well. A list of some general rules of thumb for making appropriate risk maps, taking into account these principles, will be presented.

GIS-based Decision Support Systems for spatial-oriented assessment and communication of ecological and human health risks.

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SUMMARY

During past decades, innovative frameworks and operational tools were developed in Europe and USA for the assessment and management of contaminated sites. Efforts focused on Decision Support Systems (DSS) aimed at addressing effectively the overall process from site characterization to remediation, by integrating environmental and socio-economic perspectives.

The proposed presentation compares and discusses different approaches for spatial risk assessment and management of contaminated sites, by taking as examples the experiences and related case-studies collected in the book "Decision Support Systems for Risk Based Management of Contaminated Sites" edited by Marcomini, Suter and Critto and published by Springer in 2009.

Some of the DSS described in the book make use of GIS capabilities for the spatial assessment, visualisation and communication of the risks posed by chemical stressors to human health and ecosystems, namely: MODELKEY, SYRIADE and DESYRE.

MODELKEY DSS was developed to address decision-making processes in compliance with the EU Water Framework Directive requirements. It implements MCDA-based risk assessment methodologies for environmental quality evaluation of fluvial ecosystems and prioritization of hot spots along the river basins. The MODELKEY DSS software system is implemented in an open-source GIS environment, the uDig platform.

SYRIADE is a GIS-based DSS allowing the ranking of potentially contaminated sites and mining waste sites through a relative regional risk assessment methodology in order to identify where investigation activities are urgently required. Based on an integrated assessment of physical and chemical risks and socio-economic aspects it supports the inventory of (potentially) contaminated sites at regional scale.

DESYRE is a GIS-based DSS that covers all the aspects of the remediation process and defines management options by expert elicitation and stakeholder involvement. DESYRE provides an integrated assessment of human health risks, socio-economic issues and remediation technologies selection, comparison and simulation that effectively support the risk-based management approach to contaminated site rehabilitation.

Geographically based indicator for pesticide risk

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SUMMARY

Risk indicators can act as safety net under the risk assessment by supporting risk-minimizing strategies. Such a risk indicator is developed to minimize the eco-toxicological risk due to application of pesticides. The presentation will describe the reasoning behind the risk indicator, governing assumptions and application potential.

The agricultural landscape is heterogeneous with nature elements scattered between the fields. The potential impact of pesticides on nature is assumed to depend on: (1) The spatial distance between place of application and the position of nature elements; (2) The amount, toxicity and adsorption properties of pesticides. The indicator describes the potential risk to nature due to the application of pesticides by this information in terms of toxicological pressure.

This indicator takes the consequence of the fact that indicators are relative, i.e. the indicator only relates predictions to relative risk by use of partial order theory. The descriptor of pressure is toxic pressure (number of doses) for specific impacts. The aggregation method for different potential impacts are straight forward, transparent and robust. The geographical based indicator counts “Hot spots” where several indicators simultaneously predict increased risk.

Policy makers and scientists can apply the indicator to visualise where pesticide effects are most likely to occur, which risk types are most potent, describe the time trend in risk pressures and finally also suggest best possible action taken to reduce risk.

A cumulative assessment of pesticides in Europe

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SUMMARY

We use a simple GIS-based screening model to compute pesticide concentration in soil and surface water, with reference to the full list of pesticides reported as used in agriculture in Europe. The model is based on the apportionment of used quantities of pesticide, derived from EUROSTAT reports, to land cover classes described by the Corine Land Cover 2000 map, and, subsequently, accounts for mass balance of pesticides in soils, phase partitioning, and loading to the stream network.

Comparison with monitoring data highlights the applicability and limitations of the approach, showing that it is possible to provide a first approximation of predicted environmental concentrations in soil and surface water.

We, therefore, provide an estimate of concentration for each individual pesticide, and we combine the different concentrations in a weighted summation by using ratios of a threshold concentration (such as LC50 or NOEC, depending on the endpoint considered) as weights. We show how the resulting weighted sum, an indicator of cumulative eco-toxicity, may be computed with reference to pesticide use data in different years to evaluate trends in overall pressure from pesticides at the European scale. This may be useful in monitoring progress and criticalities towards sustainable use of pesticides as required by increasing public concern and proposed European legislation.

Risks in Urbania: A showcase for novel methods to assess cumulative risk

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SUMMARY

Whereas traditional risk assessment focuses on the substance or pollution source, cumulative risk assessment puts the exposed individuals or populations at the centre of the assessment. The main aim of this Master Case is to demonstrate a manner, in which a risk assessment can be performed for people living in an urban environment and who are exposed to multiple stressors. The modeled scenario is fictional; it could be realized in the future; approximately 10 years from now. Development of a framework for such complex risk assessments will improve understanding of the effects of cumulative exposures occurring under the variety of field conditions within Europe and finally will provide a better scientific basis for forecasting risks and associated uncertainties. Moreover the Master Case study will show the coherence between different novel methods developed within the NoMiracle project.

We created a fictional city; “Urbania”, based on data and scientific methods available from different European cities. The exposure assessment was performed for 3 specific target groups, i.e. children (0-5 years), workers (18-65 years) and elderly (65 years and older). Distinction was made between (1) outdoor exposure to VOCs and PM_{10}, (2) indoor exposure to VOCs and PM_{10} and (3) exposure to pesticide residues in food. For the VOCs and PM_{10}, exposure was specified as an average daily air exposure concentration. For the pesticides in food, exposure was specified as an average daily intake. Subsequently a qualitative effect assessment was performed to identify difference in risk outcome of single stressor exposure compared to the cumulative exposure of multiple stressors.

Poster Group 1A:

Chemical fate and exposure

Chair of poster session/poster corner: Prof. Gerrit Schüürmann

Exposure of the Flemish population to brominated flame retardents

Christa Cornelis, VITO, Belgium

Exposure of the Flemish population to perfluorinated compounds

Christa Cornelis, VITO, Belgium

Modelling historical and recent human cadmium exposure in a zinc smelter area to lead in Hoboken, Belgium

Dr. Arnout Standaert, VITO, Belgium

Equilibrium sampling using Polydimethylsiloxane in fish tissue – possibilities and limitations

Prof. Philipp Mayer, Aarhus University, Denmark

Multi-media and multi-pathway aggregate exposure assessment for four phthalates in Korea

Dr. Jong-Hyeon Lee, NeoEnBiz Co., South Korea

Occurrence and fate of sulphonamide antimicrobials in different water matrices from Catalonia (Spain)

María J. Garcia, IDEA CSIC, Spain

Prediction of hydrogen bond donor and acceptor strength through quantum chemical models employing local reactivity parameters

Dr. Ralph Kühne, Helmholtz Centre for Environmental Research – UFZ, Germany

Modelling the indirect photolysis of organic compounds

Dr. Ralph Kühne, Helmholtz Centre for Environmental Research – UFZ, Germany

Exposure of the Flemish population to brominated flame retardants

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Co-authors: Smolders, Roel, Van den Heuvel, Rosette, Roosens, Laurence, Covaci, Adrian, Van Campenhout, Karen

SUMMARY

We evaluated exposure of the Flemish population to brominated flame retardants (BDE 28 through BDE 209 and HBCD) from food, settled dust (home, offices), soil and air (outdoor, home, offices, cars). Concentrations in food were estimated from food products at production level in Flanders complemented with literature values. Concentrations in settled dust were measured in homes and offices. Concentrations in air were taken from the literature. Concentrations in breast milk were determined on samples from a bio-monitoring campaign. We estimated exposure for infants (0 – 6 months, fully breast-fed) and for children (3 - 5 yrs, 6 – 9 yrs, 10 – 14 yrs) and adults. We used Flemish food consumption data and time-activity information. Soil/dust ingestion rates and inhalation rates were derived from literature. Average intake for infants ranged from 12 ng/kg.d for $\sum BDE_5$ (BDE 47, 100, 99, 154, 153) to 21 ng/kg.d at P50 and P95 concentrations in breast milk, respectively. Average intake of BDE 209 ranged from 25 to 112 ng/kg.d, whereas average intake of HBCD ranged from 0 to 15 ng/kg.d. Average exposure from food equalled 2 ng/kg.d for $\sum BDE_5$, 3.4 ng/kg.d for BDE 209 and 6.4 ng/kg.d for HBCD in children; adults take in 0.7 ng/kg.d ($\sum BDE_5$), 1.5 ng/kg.d (BDE 209) and 1.1 ng/kg.d (HBCD) as an average. Total exposure is dominated by food, although intake from settled dust (and soil for children) can become significant for the higher BDEs and HBCD at high concentrations. We compared overall intake with RfD values published by US-EPA (2008). Intake is well below the RfD values for children and adults (a factor of 50 for high intake of total BDE), but the small margin (less than 10 for high intake of total BDE) for infants indicates the need for follow-up of concentrations in breast milk.

The study was commissioned, financed and policy steered by the Flemish government (Department of Environment, Nature and Energy), who also gave conceptual framework input.

Exposure of the Flemish population to perfluorinated compounds

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SUMMARY

We evaluated exposure of the Flemish population to perfluorinated compounds from food, settled dust (home, offices), soil and air (outdoor, indoor). Concentrations in food were estimated from food products at production level in Flanders complemented with literature values. Concentrations in settled dust were measured in homes and offices. Concentrations in air were taken from the literature. Concentrations in breast milk were determined on samples from a biomonitoring campaign. We estimated exposure for infants (0 – 6 months, fully breast-fed) and for children (3 - 5 yrs, 6 – 9 yrs, 10 – 14 yrs) and adults. We used Flemish food consumption data and time-activity information. Soil/dust ingestion rates and inhalation rates were derived from literature. Exposure calculations were limited to PFOS and PFOA, due to the high quantification limits for the other perfluorinated compounds and the lack of literature data. Average intake for infants ranged from 362 ng/kg.d to 1386 ng/kg.d at P50 and P95 concentrations of PFOS in breast milk. Average intake of PFOA ranged from 35 to 105 ng/kg.d. Average exposure from food equalled 57 ng/kg.d for PFOS and 20 ng/kg.d for PFOA in children; adults take in 24 ng/kg.d (PFOS) and 6 ng/kg.d (PFOA) as an average. Total exposure is dominated by food. We compared the overall intake with TDI values published by EFSA (2008). Intake of PFOA is well below the TDI for all age groups. Intake of PFOS is above the TDI for infants and remains below the TDI for children and adults. Further research is needed to refine the intake from food (analytical methods), assess the intake from other perfluorinated compounds and the interaction effects of the different compounds as well as the critical age groups.

The study was commissioned, financed and policy steered by the Flemish government (Department of Environment, Nature and Energy), who also gave conceptual framework input.

Modelling historical and recent human cadmium exposure in a zinc smelter area – a Belgian case study

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SUMMARY

The Northern Campine region in the north-east of Belgium has a long history harboring polluting zinc industry. Most of the smelters have closed down in the last decades and the remaining factories have modernized their production processes, resulting in a significant reduction of heavy metal emissions. Despite these measures, exposure of the inhabitants of the polluted area continues.

A recent study showed a significant correlation between cadmium exposure and lung cancer incidence in the area. In order to assess the present situation concerning cadmium pollution and human exposure, a measurement campaign was set up including questionnaires, bio-monitoring for 1217 adults and environmental measurements in 100 homes.

Based on these data, we developed, implemented and validated a human exposure model. External doses of cadmium are calculated and transformed to blood and urinary cadmium level predictions using the physiologically based pharmacokinetic model of Kjellström & Nordberg. The study area was divided into different zones based on distance and wind direction from the smelters, to enable spatial differentiation in model predictions. Since urinary cadmium concentrations are a marker for lifetime exposure, the model considers the full exposure history of the participants, available through the questionnaires. The model was validated against the bio-monitoring data acquired during this campaign, and model simulations were performed for different scenarios. The contribution of different exposure routes, including local and regional foods, indoor and outdoor air, passive and active smoking, dust and soil ingestion, private well and drinking water, was investigated. The findings of the monitoring campaign and the human exposure model formed the basis for further recommendations towards population and policy makers.

Equilibrium Sampling using Polydimethylsiloxane in Fish Tissue – Possibilities and Limitations

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SUMMARY

Polydimethylsiloxane (PDMS) has been used for passive equilibrium sampling in numerous abiotic environmental matrices. Recently, this approach was extended to lipid-rich tissue. This work investigated the possibilities and limitations of using PDMS thin-film extraction for *in tissue* equilibrium sampling in fish species of varying lipid content. Polychlorinated biphenyls (PCBs) were used as model lipophilic organic pollutants. PDMS thin-films were inserted in intact fish tissue for differing time periods (1 hour up to 1 week). The thin-films were then solvent-extracted, and the extracts were analysed using gas chromatography coupled to mass spectrometry. Whether equilibrium had been established was investigated either by using PDMS thin-films of multiple thicknesses (140 to 620 µm) or by assessing kinetics by means of time series.

Equilibration was found to be rapid (i.e. in the range of hours) in lipid-rich fish, whereas equilibrium was not achieved within one week in lean tissues. Regarding lipid-rich fish, the newly developed method was found to be sufficiently sensitive to determine equilibrium partitioning concentrations of PCBs in lipids of samples from the Baltic Sea, and it is a promising approach for any kind of fatty tissue.

Multi-media and multi-pathway aggregate exposure assessment for four phthalates in Korea

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SUMMARY

Multi-media and multi-routes aggregate exposure assessment for four phthalates were conducted for total 98 individuals in different age groups. BBP, DBP, DEHP, and DINP were analyzed in several types of samples for indoor and outdoor air, house dust, dust adhering to hand, soil, food/beverage, and consumer product. In the same person, urinary biomarkers were also monitored to estimate the total exposure for the phthalates. Finally, the estimated aggregated exposures were compared with the total exposure estimated from biomarker monitoring data by dose reconstruction method. Aggregate exposure estimates (ng/kg-day) in toddler group was 1.4 ~ 5.9 times higher than those in the other age-groups; in the case of DBP, toddler (868 ng/kg-day, the median value) vs the other (217~251); in BBP, toddler (147) vs the others (30.7~106); in DEHP, toddler (4166) vs the others (708~913); in DINP, toddler (2028) vs the others (524~714). Food intake was found as a major exposure route (68.4~99.9%). Except for food exposure, dust ingestion by hand-to-mouth activity was the most important exposure route in toddler group (51.2~92.3%). Phthalates exposure by consumer products for adult and toddler groups were, respectively, 118 and 3550 ng/kg-day for DEHP, 5 and 560 ng/kg-day for DBP, 1.7 and 4140 ng/kg-day for DINP. The median daily phthalate exposures estimated from determination of urinary phthalate metabolites in toddler group were 1.2~3.9 times higher than those in other age groups; in the case of DEHP, toddler (1500~12700 ng/kg-day) vs the other (600~4900), in DBP, toddler (4000~13500) vs the other (1800~6400), in BBP, toddler (1100) vs the other (400~600). After including the exposure from consumer product, the aggregated exposure for DEHP was in the same range of the total exposure back-calculated from urinary metabolites. In contrary, the aggregated exposures for DBP and BBP were 5~100 times lower than the back-calculated values.

Occurrence and fate of sulphonamide antimicrobials in different water matrices from Catalonia (Spain)

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SUMMARY

Sulfonamides are one of the most widely used antibiotics in human and, especially, in veterinary medicine. They have been detected in all kinds of water matrices (Díaz-Cruz et al., 2008), not only because of their high consumption rates, but also to their relatively low elimination efficiency during sewage treatment procedures and to the increase in the number of confined animal feeding operations, which often lack proper waste management practices. Sulfonamides are metabolized to a considerable and varying extent in the organism, (i.e. by acetylation and hydroxilation), and these metabolites, together with the not assimilated parent substances, are excreted mainly via urine and faeces. Consequently, the extensive use of manure as fertilizer on agriculture may represent a main entrance pathway for these antibiotics in the natural media.

The present work shows an overview of the occurrence and fate of 20 sulfonamides and one acetylated metabolite in surface and ground water samples, as well as in influents and effluents of waste water treatment plants (WWTPs) of Catalonia (Spain) (for which elimination rates have been estimated). For their determination a method based on on-line solid phase extraction-liquid chromatography-tandem mass spectrometry (SPE-LC-MS/MS) was developed and applied. The sensitivity achieved with it yielded limits of detection down to the pg/L, allowing for detection at environmental levels.

The sulfonamides studied were ubiquitous in all the waters studied, in concentrations up to 1170 ng/L (sulfisoxazole in surface water). Sulfamethoxazole and sulfapyridine, mainly used in human medicine, were detected in all the WWTPs at the highest concentrations. Removal efficiencies between 30 and 100% were estimated for the seven WWTPs monitored. Regarding ground waters, the presence of the acetylated metabolite in the 80% of the samples must be highlighted (García-Galán et al., 2009).

Prediction of hydrogen bond donor and acceptor strength through quantum chemical models employing local reactivity parameters

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SUMMARY

Hydrogen bonding affects the phase partitioning of organic compounds. To predict respective partition coefficients through Abraham linear free energy relationships (LFERs), quantitative knowledge of hydrogen bond donor (HBD) and acceptor (HBA) strengths is needed. A single-molecule approach using quantum chemical parameters was applied, employing both semi-empirical and ab initio levels of computation. The HBD and HBA sites are characterized through local molecular parameters encoding electrostatic effects, polarizability, and the influence of charge transfer. Linear regression with experimental data yields values up to r^2=0.91 for the HBD model, and r^2=0.96 for the HBA model. The discussion includes a comparison with existing increment models.

Modelling the indirect photolysis of organic compounds

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SUMMARY

The major tropospheric loss process of organic compounds is the indirect photolysis with OH radicals. Respective reaction rates, thus, provide valuable information about the atmospheric persistence of xenobiotics, and are used in multimedia models for predicting their environmental exposure and fate. Post-Hartree-Fock methods have been applied to investigate the mechanism of OH radical reaction of oxygenated organic compounds. An existing nonlinear model for the estimation of OH radical rate constants is the Molecular Orbital OH (MOOH) method, developed by Klamt, which was based on semi-empirical calculations. Using an up-to-date set of approximately 800 experimental rate constants, recalibrations of the method have been carried out on both the semi-empirical and ab initio level of quantum chemistry. The method has been extended to cover more compound classes.

Furthermore, the MOOH approach has been applied to the reactions of volatile organic compounds with other atmospheric oxidants of environmental importance. The discussion includes an analysis of the dependence of the model performance on the reaction mechanism and on the level of quantum calculation, and a comparison with the prediction statistics achieved by the Atkinson increment method.

Poster Group 1B:

Effects of mixtures of chemicals and combinations of chemicals and other stressors

Chair of poster session/poster corner: Dr. Claus Svendsen

Synergy of the fungicide epoxyconazole at high and realistic concentrations, tests on *Daphnia magna*

Christina Aagaard Rasmussen, Copenhagen University, Denmark

Sensitivity of histopathology in comparison to stress proteins and other individual level tests for toxicity assessment of chemicals and chemical mixtures

Prof. Heinz Köhler, Steinbeis-Transfer Centre for Ecotoxicology and Ecophysiology, Germany

Joint effects of a binary neonicotinoid insecticide mixture in the tissues of the marine mussel (*Mytilus galloprovincialis*): a functional genomics approach

Dr. Francesco Dondero, University of Piemonte Orientale, Italy

Decision tree for the predictive assessment of compound toxicity towards *Tetrahymena pyriformis*

Dr. Ralph Kühne, Helmholtz Centre for Environmental Research – UFZ, Germany

Effect of copper on the flour beetle *Tribolium castaneum* and its resistance to the parasite *Steinernema feltidae*

Dr. Paulina Kramarz, Jagiellonian University, Poland

Interactions between anthropogenic and natural stressors – studies on the potworm *Encytreaus doerjesi*

Dr. Paulina Kramarz, Jagiellonian University, Poland

Synergy of the fungicide epoxycanazole at high and realistic concentrations, tests on *Daphnia magna*

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SUMMARY

Scientific results have shown that some ergosterol biosynthesis inhibitors (EPI), e.g. epoxyconazole, can increase the effect of pyrethoide insecticides, such as Alpha-cypermethrin. In Denmark, these two pesticides are applied as tank mixtures. In Denmark, the combination of epoxyconazole and alpha-cypermethrine is used on 20% of all wheat-fields, which is around 6% of the total Danish farming land and 4% of the total area of Denmark.

Previous studies have shown an approximately 10-fold increase in the toxicity of alpha-cypermethrine when ample Epoxiconazole is present. The question is to what extend Epoxiconazole enhances the toxicity of alpha-cypermethrine at lower, more realistic concentrations? And whether the synergy also manifests itself at sub-lethal endpoints such as reproduction and feeding rate?

This poster will present data showing the size of synergy as a function of epoxyconazole concentration. Furthermore, results from an experiment on reproduction effects at realistic concentrations of mixtures of the same two pesticides will be presented.

Sensitivity and histopathology in comparison to stress proteins and other individual level tests for toxicity assessment of chemicals and chemical mixtures

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SUMMARY

In the present project, the toxicity of six chemicals (nickel chloride, chlorpyrifos, imidacloprid, thiacloprid, diazinone, 3-4-dichloroaniline) and three binary mixtures of them were investigated with two biomarkers (histopathology, stress proteins) and two individual level test systems (ELS test, swimming behaviour) using zebrafish *(Danio rerio)* embryos as test organisms.

The results of the project made evident that histopathological investigations provide detailed information on tissue-specific effects of different chemicals also addressing the mode of mixture toxicity. Particularly in embryos and larvae or in species of small body size, they allow an overview of possible cellular targets. One of the most important advantages of histopathology is its capacity to survey the "health status" of the respective controls, i.e. to prove the validity of the tests with respect to the eligibility of the control animals.

Generally, histopathology is of intermediate sensitivity when compared to stress proteins, embryo tests and behavioural studies and turned out to be chemical-specific. For imidacloprid and 3,4-dichloroaniline, but also for thiacloprid and diazinon, histopathological endpoints were comparatively sensitive in relation to the other test parameters (table 1)

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Table 1: LOECs [µg/L] obtained in the different tests for the single substances and information on mode of interaction for the binary mixtures. Abbreviations: A: additive action; AN: antagonistic action; S: synergistic action; IA: independent action

	Stress proteins	**Histopathology (most sensitive organ)**	**Embroy test (most sensitive endpoint)**	**Behaviour (exposure time in subchronic test)**
Nickel chloride	1000	20000 (gut)	10000 (reduced hatching success)	10000 (11d)
Chlorpyrifos	100	300 (gut)	>1000	10 (5d)
Ni-CPP Mode of mixture toxicity	A (IA)	A (IA)	A (IA)	AN
Imidacloprid	1000	1000 (liver, muscle)	> 50000	1000 (11d)
Thiacloprid	500	5000 (liver)	10000 (elevated heart rate)	<40000 (5, 8, 11 d)
Imi-Thia Mode of mixture toxicity	S	AN	AN	AN
Diazinon	50	2000 (liver, muscles)	2000 (deformations)	2000 (5d)
3,4-dichloroaniline	2500	150 (gut, pancreas)	2500 (deformations)	500 (5d)
Dia-3,4-D Mode of mixture toxicity	A	A	A	A

Joint effects of a binary neonicotinoid insecticide mixture in the tissues of the marine mussel (*Mytilus galloprovincialis*): a functional genomics approach

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SUMMARY

In this study, we tested the joint effects of Imidacloprid and Thiacloprid at sublethal level (0.1-10 mg/L) in the tissues of the marine bivalve *M. galloprovincialis*. Neonicotinoid insecticides are known to act selectively on the nicotine acetylcholine receptor of insects, however, there is a lack of information on the effects on non target species (with the exception of non-pest insects, such as bees).

To test joint effects, we used a fixed design experiment based on the equitoxic effects on digestive gland lysosomal membrane stability, a well known biomarker of stress in mussels. The exposure to equitoxic amounts (1 TU according to the CA model) of the two chemicals rendered additive effects for lysosomal responses. Gill acetylcholinesterase showed two complex dynamics in the gills of mussels exposed to the two different chemicals, but the mixture effects -biased towards the outcome of thiacloprid (stimulation)- were still compatible with the principle of non-interaction among components of a mixture. To get more clues on the mode of action of the two chemicals and their mixture, we carried out a functional genomics analysis on the digestive gland tissue of mussels, by means of cDNA microarrays, real time Q-PCR and 2DE gel electrophoresis. In general, Imidachloprid and Thiachloprid displayed quite distinct molecular responses, with only five genes in common: two hsp90 sequences, the mt10 and mt20 metallothionein genes and one unknown sequence. Moreover, multivariate computations, such as Principal Component Analysis (PCA) and Self Organizing Maps (SOM), underlined differences also at quantitative level. The transcriptomic changes found in the digestive gland of animals exposed to the mixture depicted 48 differentially expressed genes, of which (19) 40% were common with either Imidachloprid or Thiachloprid samples, respectively. At the level of Gene Ontology analysis, few features were inherited from single chemical exposures such as serine-type endopeptidase activity (a molecular function) and activation of NK-b transcription factors (a biological process related to gene transcription). However, several other GO terms were significantly enriched only in the mixture samples, such as muscle development, microtuble based movement, protein polimerization, GTPase activity. These results were confirmed at proteomic level, as the three different treatments produced no overlaps. These findings lead to some relevant considerations concerning the mixture toxicity of neonicotinoid insecticide in mussels: (i) molecular responses followed only in part the principle of independent effects; (ii) a novel specific molecular signature took place from the interaction of the two compounds; (iii) imidachloprid and thiachloprid should not be considered similarly acting chemicals.

These results may contribute to explain deviations from reference systems for the prediction of mixture toxicity.

Decision tree for the predictive assessment of compound toxicity towards *Tetrahymena pyriformis*

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SUMMARY

The ciliates *Tetrahymena pyriformis* are used as alternative bioassay in both human and environmental toxicology. For the 48h growth inhibition as toxicity endpoint, we have collected approx. 1350 experimental data from literature. Employing our in-house software system ChemProp, we derived a decision tree for toxicity estimation based on mechanistic considerations. The models employs different major structural alerts representing sub-structural features, some of which contain various related subgroups. Through application of the decision tree, the structural constitution of organic compounds is analyzed in a step-wise manner, resulting in a final allocation of a given compound to one of two categories related to their intrinsic toxicological potential. The narcosis level category consists of compounds with low priority for experimental testing, because their toxicity can be predicted well through hydrophobicity-based quantitative structure-activity relationships (QSARs). Correspondingly, general QSAR models are not available for excess-toxic compounds. As a consequence, compounds allocated to this category have a higher priority for detailed investigation, the latter of which may include chemoassay analysis of electrophilic reactivity as well as non-test approaches, such as read-across and chemical category assessment, before proceeding to direct toxicity testing. A respective approach may be useful for chemical safety evaluation under REACH, exploiting information from alternative and non-test methods as much as possible and before considering animal testing.

Effect of copper on the flour beetle *Tribolium castaneum* and its resistance to the parasite *Steinernema feltiae*

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SUMMARY

Respiration rate, population growth rate and resistance to the parasitic nematode *Steinernema feltiae* were studied in the flour beetle *Tribolium castaneum* exposed to elevated copper concentrations. The experimental setup allowed also to estimate how copper affected the nematode infectivity.

The beetles were pre-exposed for 27 days (one generation) to the following Cu concentrations in the medium: 0, 0.5 and 2.5 mg kg^{-1} (nominal concentration). After this period, respiration rate was measured and animals were exposed to the same copper concentrations in a full factorial design: the beetles from each pre-exposure treatment were exposed to each copper concentration for the next 27 days. Thereafter, all individuals were counted and adults were subjected to infection with the nematodes. Three nematode treatments were used, corresponding to 0, 0.5 or 1 recommended field dose of the commercial nematode application for agricultural use. At the same time, before application, nematodes were exposed to copper at following concentrations: 0, 200 or 800 mg l^{-1}. The experiment was performed in a full factorial design – the beetles from each copper treatment were infected with each dose of nematodes originating from each copper concentration.

No influence of copper on the beetles respiration rate was observed - the only noted difference was between sexes. Population growth rates of the beetles pre-exposed to copper were more affected by the next intoxication with copper than in the case of animals not exposed to Cu before. Similarly, pre-exposed *T. castaneum* were more vulnerable to infection with nematodes, revealing the highest mortality among all treatments. Copper had also negative impact on the nematodes infectivity.

The studies were performed under the EEA grants FRISC and project of Polish Ministry of Science and Higher Education Nr N N304 027334.

Interactions between anthropologenic and natural stressors – studies on the potworm *Enchytreaus doerjesi*

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SUMMARY

Pollutants are only seldom present in nature as a single factor, and more often organisms are actually exposed to mixtures of different stressors – natural and anthropogenic. Herein we present results from a set of experiments performed on the easy to culture potworm species *Enchytraeus doerjesi* and concerning its response to mixtures of stressors. All studies were performed under the EU 6th Framework Project "NoMiracle".

Each full factorial experiment consisted of an interaction between two factors: one toxicant and one natural. The investigated chemicals were: two metals, nickel (Ni) and copper (Cu); two pesticides, chlorphyriphos (CFP) and abamectin (ABA); and one polycyclic aromatic hydrocarbon, phenantrene (P). Natural factors were: drought (expressed as % soil water holding capacity, WHC), temperature (T), food limitation (F), and pH. The following interactions were studied: Ni×WHC, Ni×T, Ni×F, Ni×pH; CFP×WHC, CFP×T, CFP×F, CFP×pH; Cu×WHC, ABA×WHC, ABA×T, P×T. The animals were exposed to the studied factors for 28 days (ca. one generation). Each factor was applied in at least five levels at five replicates, and the main endpoint was the instantaneous population growth rate (r_i).

All toxicants alone affected negatively the population growth rate of potworms, and suboptimal level of the natural factors caused a decline in $r_{i,}$ exhibiting in many cases parabolic relationship. Significant interactions between two factors were observed for: CFP×WHC, CFP×T, ABA×T, P×T, Ni×pH, CFP×pH. The observed complex curvilinear relationships of r_i on combined effects of toxicants and natural stressors make them difficult to predict from standard eco-toxicological tests. We suggest thus to include at least some most important natural factors in standard eco-toxicological tests.

Poster Group 2A:

Cumulative risks in complex systems

Chair of poster session/poster corner: Dr. Ad Ragas

Assessing and mapping pesticide risk on ecosystems. I: epygean terrestrial communities - pollinators

Stefania Barmaz, University of Milano Bicocca, Italy

Assessing and mapping pesticide risk on ecosystems. II: epygean terrestrial communities - birds

Dr. Serenella Sala, University of Milano Bicocca, Italy

Assessing and mapping pesticide risk on ecosystems. III: soil community

Dr. Claudia Vaj, University of Milano Bicocca, Italy

Macroinvertebrate community structure along gradients of physical stream quality and pesticide load in Danish streams – a methodological description

M.Sc. Jes Rasmussen, Aarhus University, Denmark

Impact of pesticides on microbial leaf processing and macroinvertebrate shredding activity

M.Sc. Rikke Monberg, Aarhus University, Denmark

HEIMTSA: Health and Environment Integrated Methodology and Toolbox for Scenario Assessment

Dr. Brian Miller, Institute of Occupational Medicine, UK

Chlorpyrifos and neurodevelopmental toxicity: Critical assessment and expert elicitation

Dr. Brooke Magnati, Bristol Haematology and Oncology Centre, UK

HENVINET Networking Portal: Web community joining health and environment professionals

Dr. Alena Bartonova, NILU Norwegian Institute for Air Research, Norway

Do we know enough? Knowledge evaluation in environmental health: The HENVINET methodology

Dr. Alena Bartonova, NILU Norwegian Institute for Air Research, Norway

Assessing and mapping pesticide risk on ecosystems. I: epygean terrestrial communities - pollinators

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SUMMARY

Official procedures to assess agrochemical risk for pollinators are based, at least in the first tier, on the HQ, the ratio between application rate (g/ha) and LD_{50} for *Apis mellifera*. Any quantification of actual exposure is considered. Starting from these issues, a methodology to assess exposure and risk for pollinators was developed, calibrated and validated in different 4x4 km field sites selected as representative of the main European cultivated crops and meteo-climatic conditions. Exposure in terrestrial ecosystems depends on the environmental fate of active ingredients, but also on organisms' behaviour. Pollinator activity is, generally, concentrated in the productive season. The radius of the area visited daily by bees may reach 1km and the amount of pollen eaten daily may reach from 1 to 6 milligrams. Exposure depends on the social role and the growth stage; *larvae* are exposed orally whilst worker bees are exposed mainly by contact. The probability of exposure is strictly linked to crop attractiveness for bees. Application during the flowering period is generally avoided, for this reason pollen, flowers and foliage of non crop species could be considered as the main matrices involved in exposure in agroecosystems. Starting from these issues, the PEC (Predicted Environmental Concentration) for the main active ingredients used in the studied sites was calculated. The obtained predictions were validated with monitoring data. Then, the TDI for *Apis mellifera* was integrated with ecotoxicological acute endpoints to characterize and map risk for pollinators community. The possibility of additive effects was evaluated using the Concentration Addition model in order to evaluate the toxicological potency of mixtures. A validation of risk predictions with data on pollinators communities, considering the contribute of multiple stressors, is ongoing.

Assessing and mapping pesticide risk on ecosystems. II: epygean terrestrial communities - birds

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SUMMARY

In agro-ecosystems, natural communities are affected by several potential stress factors. The risk assessment procedure related to bird communities presents a number of critical aspects. At present, the Guidance Document on Risk assessment for birds and mammals and the current methods to perform eco-toxicological risk assessment take into account pesticide properties (application rates and patterns, physical-chemical properties) and bio-ecological characteristics of birds (weight, feeding rates, ecology and behaviour, role in the food chain). However, a site-specific approach is required to perform a refinement of the risk assessment at different scales, taking into account several critical issues related to the risk assessment procedure (availability of toxicological data, extrapolation of toxicity data, choice of focal species etc). A Gis-based risk assessment procedure was proposed to up-scale the approach. Detailed information on landscape and agriculture (land use, pesticide application, etc.) was available, and the structure of the bird community was experimentally determined through field observations. In this study, an application is presented and critical issues related to the results are discussed.

Assessing and mapping pesticide risk on ecosystems. III: soil community

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SUMMARY

In agricultural practices a large number of plant protection products (PPP) are used, and a fraction of them fall onto the soil during the application. Thus, soil and its community are exposed to complex mixtures of active ingredients, usually with different chemical and eco-toxicological characteristics, applied to the crops. The transport pattern by which pesticides reach soil is mainly drift, thus, the area exposed to agrochemicals is only in the proximities of the crop on which they are applied.

Soil shows high differences as environmental compartment compared to air or water, because it is almost immobile. This means that there could be great differences of PPP mixtures in few meters due to different application patterns between crops and even fields of the same crop. Movements of substances are very low and the exposure of soil community is mainly related to organisms' behaviour, their movements (for big organisms, as earthworms) or their adaptation to soil (for smallest species, as springtails).

The mixture to which soil is exposed changes in time due to the application patterns and substances degradation times, posing different risk also in relation of organisms' life cycles and community changes during the seasonal cycle.

Procedures to assess pesticide risk to soil communities were developed and applied to a real case, a vineyard in Northern Italy. Changes in time during an annual cycle have been taken into account.

Due to soil characteristics, the focus scale for mapping risk is very small in the proximities of the source of pollution (i.e. crops). An example of risk mapping is given and it's related to the possibility of producing GIS-based maps of risk. The major critic points of the procedure will also be highlighted.

Macroinvertebrate community structure along gradients of physical stream quality and pesticide load in Danish streams – a methodological description

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SUMMARY

A wide array of pesticides are applied to agricultural crops during the spring and autumn spraying season, and detections of pesticides in stream water and bed sediments of agricultural streams emphasize the potential exposure of benthic macro-invertebrates. Major transportation routes from catchment to stream are surface runoff and tile drainage, giving rise to short pulses of acute contamination strongly coinciding with high levels of precipitation.

Field studies indicate that macro-invertebrate community structure can be impacted by pesticides during spraying seasons in May and June, but also that it is difficult to disentangle the specific effects of pesticides from those related to the poor physical conditions prevailing in the majority of agricultural streams. This study aims to contribute to separate the effects of pesticides from those of poor physical conditions.

Model based predicted pesticide loss to streams was calculated for 1 km^2 catchments (produced from topographical maps) on Funen, Denmark. The physical condition (substrate, meandering etc.) of 1^{st} and 2^{nd} order streams (based on existing data from the National Monitoring Programme and personal exploring) draining these catchments was, additionally, assessed. Subsequently, 15 small streams were selected, representing different expected pesticide loading. In each stream, two successive reaches differing in physical properties (upstream reach characterised by poor and downstream by good physical conditions) was selected. In the spring 2009, the pesticide contamination in each stream was measured applying sediment sampling and event triggered water samplers. Furthermore, on all reaches macro-invertebrate community structure was assessed before, during and after the spring application season. Stream reaches with good physical quality generally contain a higher abundance and species richness of EPT taxa and we, therefore, hypothesize that reaches with good physical properties are more sensitive to acute pesticide contamination (measured as the frequency of SPEcies At Risk) than reaches with poor physical properties.

Impact of pesticides on microbial leaf processing and macro-invertebrate shedding activity

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SUMMARY

Pesticides are frequently applied in agricultural catchments and subsequently transported to stream recipients through e.g. tile drainage and surface runoff. This gives rise to short pulses of pesticide contamination in the stream, where lipophilic compounds rapidly adsorb to organic matter, consequently impacting stream dwelling organism feeding on the organic material.

The impact of pyrethroid insecticides on stream macro-invertebrates are well studied, and increased mortality and drift rate along with decreased feeding activity are well known responses to even very low concentrations (10-100 ng/L). However, the potential impact of pesticides on aquatic microbes is probably equally important. Microbial organisms are essential in organic matter breakdown, and their growth additionally increases the food quality of organic matter for macro-invertebrates. Consequently, pesticides impacting microbial organisms have the power to reduce organic matter breakdown and food quality for macro-invertebrates, thereby decreasing ecosystem decomposition rates.

We exposed preconditioned leafs of beech (*Fagus sylvatica*) to the fungicide propiconazole (100, 1000 or 2000 µg/L) and/or the insecticide alpha-cypermethrine (100, 1000 or 2000 ng/L) for three hours. Subsequently, we studied post exposure leaf degradation for four weeks in the laboratory in the presence/absence of two macro-invertebrate shredders (*Gammarus pulex* and *Halesus radiatus*) applying a classic crossed factorial design. Preliminary results indicate decreasing microbial litter processing with increasing concentrations of either propiconazole or alpha-cypermethrine. Additionally, the binary mixture further reduced microbial litter processing compared to single compound exposures. A similar reduction in leaf litter processing was only evident during the first post exposure week when macro-invertebrate shredders were present. After four weeks, no differences were apparent among treatments, indicating a strong degree of functional redundancy applying this macro-invertebrate assemblage.

HEIMTSA: Health and Environment Integrated Methodology and Toolbox for Scenario Assessment

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SUMMARY

We describe the HEIMTSA project funded under EU FP6. Its aim is to extend available health impact assessment (HIA) and cost-benefit analysis (CBA) methods and tools to the extent where it is possible to evaluate, at the European level, the environmental impacts of real-life policy scenarios. Sectors covered include transport, energy, agriculture, industry, households, and waste treatment and disposal.

HEIMTSA uses the 'full chain' or 'impact pathway' approach. It will follow the effects of policies from emissions to air, soil and water, through changes in environments and human exposures, to impacts on health and their monetary value.

We describe the various component work streams, how they link together, and a number of case studies planned to develop and test the tools and their integration. The poster will also highlight the increasingly close collaborative links with other FP6 projects, especially INTARESE and 2-FUN, and including also NoMiracle.

Chlorpyrifos and neurodevelopmental toxicity: Critical assessment and expert elicitation

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SUMMARY

Organophosphate (OP) compounds are used worldwide in agriculture and gardening to control insect pests. They also have residential and indoor applications for pest control, especially for cockroaches and termites. OPs act by inhibiting acetylcholinesterase, thus affecting nerve function in insects, humans and other animals. Most of the animal and human studies published between 2000 and 2007 refer to the OP chlorpyrifos (CPF).

There are concerns about the safety of CPF in the environment. While previous studies have shown levels of CPF that are safe in adult animals, recent evidence indicates young animals and humans may be more sensitive to CPF toxicity. In young animals, CPF is neurotoxic and mechanistically interferes with cellular replication and differentiation. This leads to alterations in the synaptic transmission in neurons.

OPs are used frequently in Europe for pest control due to their low price and broad spectrum of activity. In 2003 they accounted for over 59% (4645 tonnes) of insecticide sales in the EU, with CPF the top selling insecticide (15.6%, 1226 tonnes). CPF was also one of the most widely used OPs in the US for pest control, but the US Environmental Protection Agency imposed a ban on the sale of CPF for residential use in December 2001.

The consideration of whether to ban OPs for domestic use in Europe is a complex process involving both health and lifestyle considerations. Moving from scientific data to policy interpretation is a nontrivial challenge, because public health risks are scientifically very complex. Scientific assessment of environmental health risks is faced with large, sometimes irreducible, uncertainties, knowledge gaps, and imperfect understanding, and may also have conflicting claims and scientific controversy.

In order to better inform policymakers of the scientific basis of any proposed action, an expert elicitation was undertaken to identify areas of the research in need of further examination. This study considers the environmental health effects of CPF exposure *in utero* and during childhood and its relationship with neurodevelopment. The results will be used to form the basis of a decision support tool which has the aim of preparing policymakers with the necessary scientific background to address the concerns surrounding OPs and their applications in the home.

HENVINET Networking Portal: Web community joining health and environment professionals

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SUMMARY

The HENVINET project has the primary goal to support informed policy making by integrating environment and health issues, for the greater purpose of protecting the health of populations and individuals. To facilitate this integration, the project has created a networking portal which is designed specifically for joining the global environment and health community. With a range of innovative tools for locating and accessing expertise, sharing knowledge, views and networking with peers, HENVINET empowers a multi-stakeholder approach to addressing the most pressing environment and health issues at hand. The HENVINET portal provides environment and health professionals and stakeholders anywhere in world with the ability to:

- Network with peers: Engage with a community of scientists, policymakers and stakeholders to share expertise, views and information.

- Access the experts: Search for and pinpoint specific expertise, and efficiently communicate and discuss concerns and specific topics with renowned experts.

- Tackle global challenges: Effectively collaborate within self-forming communities and forums that bring together a relevant portfolio of experts and stakeholders to address the issues at hand.

- Set the agenda: Shape the agenda of the Environment and Health community by participating in communities and forums discussing hot-topics of today and tomorrow.

- Share opportunities: Advertise conferences, symposia, research calls, job opportunities and the like to a broad range of professionals.

The networking components of the portal will be presented, along with how these components are envisioned to join environment and health professions in an interactive web-based community.

Do we know enough? Knowledge evaluation in environmental health: the HENVINET methodology

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SUMMARY

Prioritizing research or management needs is a task that involves a significant input from experts, as we need to assess the knowledge base that underpins our decisions. Only few methods involving systematic knowledge evaluation are widely used. HENVINET designed and implemented such methodology for a number of environmental health issues based on the priority areas of the Environment and Health Action Plan, in broad categories the asthma and allergies, cancer, neurodevelopmental disorders and endocrine disruption.

The methodology involves a combination of scientific review and expert evaluation. First, each identified issue is translated into a schematic framework: it can be illustrated by a causal chain diagram or a mind-map that identifies the links between environmental change and its consequences on health. Based on the diagram, we develop a web-based questionnaire to ask experts to assess the diagrams completeness and accuracy, and the state of knowledge in each element and link. As a final step, the experts need to analyze and interpreted agreements and disagreements in their answers, and based on the results, suggest prioritized actions. Statistical consensus measures are used to summarize the results of the evaluation, which often requires answering a large number of individual questions.

Six diagrams are available for expert evaluation through our web site, and other are being prepared. As an example of assessment results, the evaluations for Climate change and respiratory health show that of the eight determinants of respiratory health related to climate change (dampness, molds, heat waves, cold exposure, surface ozone, particulate matter, pollen and dust mites), least knowledge exists on particulate matter. Usually, recruitment of experts for the evaluation is difficult: each diagram has been evaluated by between 12 and 25 experts, and about half then attend the final workshop. The final workshop has so far been carried out for three issues.

Poster Group 2B:

Risk perception, risk communication and assessment-governance links

Chair of poster session/poster corner: Prof. Mikael Hildén

Concepts, barriers and opportunities for integrated risk assessment and management: Insights from interviews with EU chemical regulators and stakeholders

Dr. Timo Assmuth, Finnish Environmental Institute, Finland

Innovation in integrated risk assessment and governance: A conceptual model

Dr. Timo Assmuth, Finnish Environmental Institute, Finland

Cultural types in integrated approaches to cumulative risks

Dr. Timo Assmuth, Finnish Environmental Institute, Finland

Communication needs of chemical risks – a consumer/public perspective

Dr. Christina Benighaus, DIALOGIK, Germany

Risk governance from cumulative stressors

Dr. Christina Benighaus, DIALOGIK, Germany

How to deal with multiple stressors in soil management issues

Dr. Marlies ten Hove, Soil Protection Technical Committee, The Netherlands

Concepts, barriers and opportunities for integrated risk assessment and management: Insights from interviews with EU chemical regulators and stakeholders

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SUMMARY

Based on 16 semi-structured interviews, we studied views of EU regulators and stakeholders on integrated risk assessment (IRA) and management. A variety of interpretations of IRA and cumulative risks of multiple stressors were observed, reflecting different ways of framing risk assessment and management: some views were based on beliefs that risks can be largely known and controlled, even if their multiplicity was seen as a major challenge, while others were grounded in a more explicit awareness of uncertainties and ambiguities in risks and their management. Notwithstanding this variety, the material allowed to discern, at a general level, some commonalities in the framing of integrated assessment, converging around two key notions: 'more realism in risks' and 'manageable approaches', i.e. more realism in procedural change, in dealing with complex risk issues. Interviewees repeatedly expressed the concern that integrated approaches should not become too complicated and irrelevant for management. Perspectives on IRA are seen as depending largely on the balance between these approaches. We generally distinguish between a pragmatist, stepwise approach, stressing 'manageability' and formalism and focusing on the limited openings for integrated approaches in rigid current regulatory frameworks (e.g. REACH); and a more ambitiously integrative and evolutionary approach that sees more possibility for complex assessments in the context of flexible (but often weaker) frameworks (e.g. land use planning, Water Framework Directive, some areas of risk governance). The results allowed us to identify and characterize conceptual, structural and functional barriers for the development and uptake of IRA and ways to overcome these barriers, such as priority-setting and working principles for linking this development and application of IRAs with their use contexts.

Innovation in integrated risk assessment and governance: A conceptual model

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SUMMARY

We developed a conceptual model of innovation in integrated risk assessment based on extant models of processes in innovation, and utilizing empirical and evolutionary theories of innovation in the policy sphere. Innovation is defined broadly as the practical application of new knowledge, methods and procedures. On a multi-dimensional reading of R&D, application and knowledge, we specify functional relationships between innovation, risks and assessment, focusing on innovation in risk assessment and governance, not as usual on assessment of risks from (or to) innovation. We address innovation at several levels in R&D and in governance, in both domains including experimentation and learning. We investigate methodological research as a vehicle of innovation in the risk field in scientific and policy terms, and how it relates to regulatory and overall social pull and push factors (Fig. 1). We emphasize pull models that have advantages over more common and rigid push models when systems are non-specified and not steered by control-and-command, and information is ambiguous, a situation common in risk governance. We note that the system is not orderly but involves randomness, unpredictability and co-evolution, and distinguish between permanent and transitory barriers of innovation and integration. We illustrate the conceptual model with some appraisals of the EU R&D and governance systems and of their interplay, within integrated risk assessment and management of chemicals and related fields.

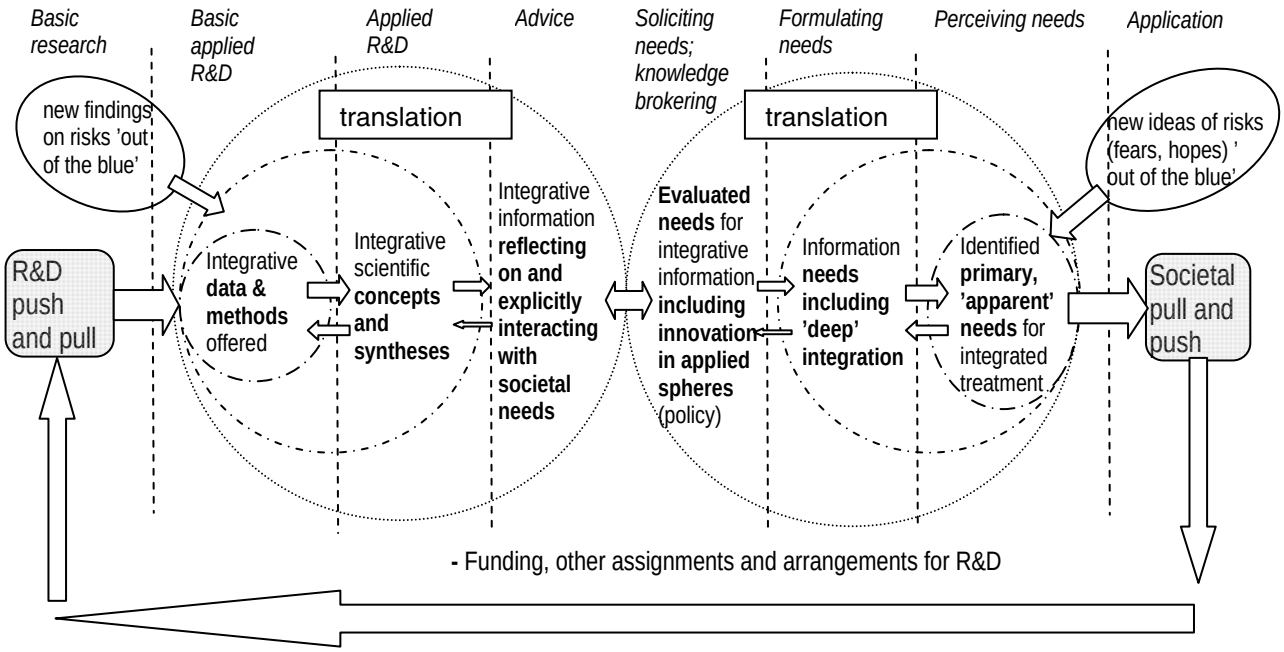

Fig. 1. Innovation 'push' and 'pull' between R&D and perceived societal problems and drivers, for different levels of integrated risk assessment. Note that the levels overlap and involve feed-backs and that the barriers between areas of integration and innovation are not firm.

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Cultural types in integrated approaches to cumulative risks

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SUMMARY

Starting from the social grid/group affinity model of cultural prototypes in risk perception proposed by Douglas and co-workers at the turn of 1980's and applications and discussions of this model, we examine socio-culturally grounded overall conceptions and views of cumulative risks from multiple stressors and their integrated assessment in contexts of methodological innovation for assessments. We examine how novel approaches to integrated risk assessment fit with studies of expert and stakeholder views of such approaches. We show that prototypes such as 'egalitarians', 'entrepreneurs', 'bureaucrats' and 'hermits' cannot fully describe the views of actor groups like regulators, experts, industry and NGOs. There is large internal variation in their concepts and positions, and the prototypes, together with other broad categories, offer only first hand heuristic devices to grasp views of and responses to risks. In integrated risk assessment, the challenge of multiple risks transforms the prototypes as additional cultural orientations become involved. Tensions can be noted between optimistic and pessimistic views of objective and broad knowledge in dealing with complexity and uncertainty in risks. Conservative views of integrated risk assessment tend to emphasize measurable facts; other views stress valuations and asymmetries in risk perception, even seeing integration as a chimera and threat. We find such additional categories play a role in balancing integration with specification and novelty with tradition. We conclude that more reflexive deliberation is required and that a key challenge for novel methods for cumulative risk from multiple stressors lies in supporting such deliberation and social learning.

Communication Needs of Chemical Risks – a Consumer/Public Perspective

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SUMMARY

The consumers' perception of risks in everyday life differs from experts' views and their judgement. The views on risks also differ among the consumers. What drives the perceptions of chemical risks and how can communication be designed to address the heterogeneous concerns of different consumers? The crucial question of communication, concerning the what, how, through which channels and by whom still awaits systematic and scientifically valid answers.

In order to gain knowledge about the communication of chemical risks and combined risks, DIA organised and conducted three focus groups, two with engineering students and one with mothers with young children. The main objectives were to demonstrate the variability of the consumers' behaviour and needs and explore the mechanisms of coping with complexity, uncertainty and ambiguity. The results confirmed the variability of answers and provided rich empirical data of which aspects should be taken into consideration when communicating chemical risks.

Risk Governance from cumulative stressors

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SUMMARY

The poster introduces an integrated analytic framework for risk governance which provides guidance for the development of comprehensive assessment and management strategies to cope with risks, in particular with cumulative stressors. The framework integrates scientific, economic, social and cultural aspects and includes the effective engagement of stakeholders.

The concept of risk governance comprises a broad picture of cumulative risk stressors: not only does it include what has been termed 'risk management' or 'risk analysis', it also looks at how risk-related decision-making unfolds when combined exposures to multiple stressors are involved, requiring co-ordination and possibly reconciliation between scientifics, perspectives, goals and activities.

The framework's risk process breaks down into three main phases: 'pre-assessment', 'appraisal', and 'management'. A further phase, comprising the 'characterisation' and 'evaluation' of cumulative risks, is placed between the appraisal and management phases and, depending on whether those charged with the assessment or those responsible for management are better equipped to perform the associated tasks, can be assigned to either of them – thus concluding the appraisal phase or marking the start of the management phase. The risk process has 'communication' as a companion to all phases of addressing and handling risk and is itself of a cyclical nature.

How to deal with multiple stressors in soil management issues

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SUMMARY

Recently, the Dutch regulations for soil management and remediation of contaminated soil have been revised. The changes in the framework dealing with contaminated sludge and soil focus on an integral approach between the environmental compartments and a risk-based approach related to the site-use. Several risk-based standards in the framework include new elements regarding e.g. combined toxicity.

As well as in standard setting as in the evaluation of a specific site, it is possible to deal with combined toxicity. Standard setting till now is dealt with combined toxicity via the so-called 'group and sum norms' e.g. for PAH's.

For the decision making about the necessity of remediation of contaminated sites in the Netherlands, a so-called 'Remediation Criterion' is available. Within this criterion, a risk assessment is made in a standard way. The Soil Protection Technical Committee, TCB did a proposal how to integrate combined toxicity for humans in the 'Remediation Criterion'. In this proposal the working mechanism of substances plays an important role.

For the eco-toxicological risk assessment within the 'Remediation Criterion', the National Institute for Public Health (RIVM) has formulated a proposal based on a mixture of chemical contaminants. This proposal is meant for both the standard risk assessment, and for a site-specific assessment.

Another example of assessing combined effects in the 'Remediation Criterion' is via the TRIAD approach. The method means to optimize the estimation of actual ecological effects in a specific area or ecosystem. The TRIAD approach includes three pillars consisting of chemical toxicological and ecological measurements. Each pillar of the TRIAD approach can be extended over three tiers, representing low, middle and high levels of sophistication.

The examples mentioned above focus on combined toxicity and not on multiple stressors. The question is: Would it be possible to deal with multiple stressors in soil management issues?

Introduction to panel discussion

Dr. Ad Ragas

The most used methods in assessing effects of mixtures (Concentration Addition and Effect Addition) are effect based and not process based. They are data-demanding and have severe limitations for the extrapolation potential and for the interpretation of experimental data. Therefore these methods are of limited use to assess effects of complex mixtures as we encounter them in our environment. A novel process-based method includes exposure duration in a more efficient way, however, requires revision of current test guidelines in terms of time dependent observations. The scientific and regulatory advantages and drawbacks by using the novel concept are illustrated by a case study showing how the alternative organism based approach was successfully used to assess the effects of mixtures under natural conditions?

AUTHOR INDEX