

# SETAC-NoMiracle International Workshop on Mixture Toxicity

By Hans Løkke, Claire Mays and Morten Strandberg



Venue of the SETAC-NoMiracle workshop in Krakow April 2-6, 2006.

Photo: Susana Loureiro

On April 2-6, 2006 in Krakow, Poland, SETAC Europe and NoMiracle held a workshop on Mixture Toxicity, focusing on the state of the art of mixture toxicity research and its use in environmental and human health risk assessment. SETAC is the worldwide Society of Environmental Toxicology and Chemistry. The workshop was attended by 31 invited experts from USA, Canada and Europe, representing academia, industry and governmental agencies.

The President of SETAC Europe, Dr. Fred Heimbach and the Co-ordinator of NoMiracle, Dr. Hans Løkke actively participated in the workshop. The NoMiracle Newsletter asked Dr. Hans Løkke to give his impression of the event:



The Co-ordinator presents how NoMiracle contributes to the EU Environment and Health Action Plan.

Photo: Ryszard Laskowski

1. SETAC-NoMiracle International Workshop on Mixture Toxicity
5. Ecological and human health risk assessment workshop – *Second announcement*
6. NoMiracle contributions at SETAC 2006, The Hague May, 7–11
8. International School on Environmental Risk Assessment – *First announcement*

### Why did NoMiracle organise the Mixture Toxicity Workshop?

There are at least three reasons why it was important to organise this workshop. Firstly, Mixture toxicity is a major challenge for scientists and regulators. Living organisms are always exposed to mixtures of chemicals. Due to the infinity of possible combinations of chemicals and ambient concentrations, simple testing is no way solving the problem. Therefore, it is very important to develop concepts and models based on available data and information in a broad international collaboration between regulators, industry and academia.

Secondly, one of the major innovations of NoMiracle is seeking to integrate human and environmental risk assessment. Usually those types of assessment are separated. As well, we need to develop mutual understanding and check that the terms used by scientists in one area are meaningful for those in the other. This workshop was in fact the first attempt worldwide to bring renowned human and environmental experts together in a workshop aiming at the elaboration of common shared concepts. Our participants exchanged views on the current state of the art, across Europe and America, academia, regulators and industry.

Last but not least, key scientist scientists from other related EU projects were attending the workshop, ensuring proper transfer of knowledge across projects.

### The workshop was organised together with SETAC Europe – *How did this come about?*

First and foremost we were informed around New Year 2006 that SETAC Europe planned to hold a workshop similar to the one already programmed by NoMiracle. Clearly many scientists have felt the need for this kind of encounter! I found it fascinating to collaborate with SETAC rather than blindly hold two separate mixture toxicity work-

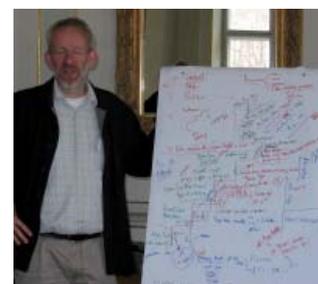
shops in Europe. SETAC represents the largest network of environmental chemists and toxicologists in the world, and I saw that this would open many possibilities to compose a strong team of experts. I phoned to Fred Heimbach (President of SETAC) and the Director of SETAC Europe, Dr. Bart Bosveld. Both were enthusiastic about the idea. We had the logistics ready in Poland, thanks to our local NoMiracle Organising Committee, and the Scientific Committee of the NoMiracle Workshop had prepared the preliminary list of invited experts. Fred joined the Committee and the list of participants was expanded with experts from USA and industry. Unfortunately we had too short time to seek funding, but most of the invited participants found the workshop so important and challenging that they decided to come to Krakow without external funding.

### Which benefits are expected from the cooperation with SETAC?

First of all we benefited from gathering so many outstanding scientists from across the world to work on an issue important for NoMiracle! Combining the SETAC and NoMiracle dissemination platforms will allow us to reach a much larger scientific audience. And all those who read about the workshop results will learn about the NoMiracle activities regarding chemical mixtures.

### How did the workshop unfold?

The programme was prepared carefully by Dr. Kees van Gestel from NoMiracle in collaboration with the Scientific Committee members, all of whom attended the workshop. Kees also chaired the workshop in a brilliant way, orchestrating a complicated schedule. During the



Leo Posthuma from RIVM, the Netherlands: "Did I say simple?"

Photo: Ryszard Laskowski



Kees van Gestel from NoMiracle chaired the workshop. Photo: Ryszard Laskowski

day, separate groups worked in parallel on five topics that are important for grasping mixture toxicity whether for humans or for other organisms found in our environment. These are:

- exposure (how to measure the amounts of chemicals that may enter the living organism)
- kinetics and metabolism (how the chemicals travel within the organism and how they are “digested”)
- toxicity (what are their negative effects on the organism)
- test design (how to measure the effects of mixtures)
- risk assessment (to man and environment).

In the evening sessions the hard work of the day was presented to the plenum and exposed to harsh critiques, which might have blown the speakers out of the windows had they not been based on solid scientific ground.

Very little time was left for enjoying the excellent site, a Polish manor house, well equipped for housing an international workshop. The Polish colleagues did a wonderful job of organising, including a workshop dinner in old Krakow.

### What is the concrete output of the workshop?

During the workshop the first draft of a booklet was produced, including recommendations for further research and development (see Box 1). It is our intention to finalise this book during the coming months, relying on the continuing collaboration of all the expert co-authors. Depending on the organisers’ success to achieve funding for printing, we hope to see the booklet printed and distributed by the end of 2006.

#### Box 1

### Draft recommendations SETAC/NoMiracle Workshop on Mixture Toxicity, April 2-6, Krakow, Poland

#### Exposure

1. Generate emission data that may help better estimate mixture exposure.
  - a. Collection of data on existing chemicals should be evaluated to determine if it is fit for purpose for mixture scenario prediction.
  - b. International collaboration for exchanging emission data.
  - c. There is a special need to consider emission of new and emerging chemicals, e.g. nanotechnology.
2. Prioritise emission mixtures to focus on most common and most relevant mixture emissions scenarios.
  - a. Large scale monitoring programs e.g. global programs such as AMAP, EMEP-ECE should include old and new chemicals and focus on mixtures.
3. Studies on fate in the environment should include aspects that cause a change in mixture composition from emission until exposure.
  - a. Models that describe distribution of mixtures in the environment need to be validated.
4. Research on potential interactions between individual chemicals that might affect the exposure, availability or toxicity of the mixture.
5. Monitoring programmes measuring total concentrations should include measures of parameters (environmental characteristics e.g. clay, organic carbon content, pH, DOC) and physical chemical properties of compounds that help to evaluate bioavailability.
6. Research is needed to assess if it is possible to extend integrated models that link exposure-toxicity (like the BLM) for use with mixtures.

*(continues on next page)*

7. Improve methods for identification of the probabilistic distribution of short and long-term exposure of possible chemical mixtures for ecosystems and humans.
8. Generate data that may help better estimate mixture exposure.
  - a. Analytical methods should be available for new chemicals coming onto the market (e.g. as for pesticides).
  - b. Differentiate between simultaneous and subsequent exposure.
    - Long-term trends at the same locations.
    - Spatial sampling at the same time.
  - c. Better understanding of routes of exposure, potential entry and exposure of humans to new chemicals and their contribution to mixtures.
9. Improve prediction of exposure for different life-stages of humans for chemical mixtures accounting for behaviour patterns.

### Kinetics

1. More kinetics/dynamics modelling in (eco)toxicology.
  - a. Help designing experiments.
  - b. Ultimately minimises testing.
2. Refine existing models to deal with mixtures.
3. Gathering of information on the conservation (throughout the animal kingdom) of physiological and biochemical mechanisms. Such information may help in extrapolating results obtained for one species to other species.
4. Experimental requests.
  - a. Parallel determination of kinetics and toxicity.
  - b. Determine toxic effects of mixture in time.
5. Complex questions justify complex models.

### Risk Assessment

1. Guidance (not guidelines!) on Risk Assessment of mixtures should have some more "regulatory" weight (it should not only be in a scientific book):
  - a. EU: Human and Environmental Risk Assessment.
  - b. USA: Environmental Risk Assessment.
  - c. Guidance should be subordinate to other/existing/overarching regulations (e.g. protection levels are determined somewhere else).
2. We need better criteria/indicators to include interactions in the Risk Assessment of mixtures:
  - a. Molecular mechanisms (especially Environmental Risk Assessment).
  - b. Reaction networks.
  - c. Organ interactions (human).
  - d. Population level.
  - e. Community level.
  - f. Both types of interaction should be addressed: synergistic (precautionary) / antagonistic (realism / not to be over-protective).
3. Toxicological, chemical & statistical criteria for establishing sufficient similarity of mixtures are needed.
4. Conduct research to support the assumptions made in mixtures Risk Assessment:
  - a. Similarly shaped Dose-Response-curves.
  - b. Fundamental theory development needed for Modes/Mechanisms of Action on different levels of biological organisation:
    - Molecular mechanisms.
    - Reaction networks.
    - Organ interactions (human).
    - Population level.
    - Community level.

Research needed to quantify the risk of the default models (response & effect addition) being insufficiently protective.



Final deadline for registration  
**May 20, 2006**

The aim of the workshop is to discuss the composition and usage of criteria for the selection of risk scenarios, mapping and visualizing risk, and communicating it to the general public, the decision makers and scholars in other disciplines.

During the workshop, a series of examples will illustrate the main topics and introduce discussion among the participants.

Discussion sessions will allow all participants to present experiences and research related to the workshop topics.

**Main Topics:**

- Scenario screening to support risk assessment
- Geographical risk mapping
- Communication of methods to users: presentation of experiences in mapping of risks;
- Highlighting the potential implications for application of the precautionary principle.

**Target groups of participants:**

- Scientists: GIS mapping, Eco-system, Human health, Eco-toxicity, Risk assessment and management
- Decision makers at a technical level
- Industry
- SME's
- NGO's
- International organisations

**Organisation:**

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For more information and program in full see:  
NoMiracle web page: <http://nomiracle.jrc.it>

# NoMiracle contributions at SETAC 2006, The Hague May 7–11

By Morten Strandberg

The presence of NoMiracle at the SETAC Europe Conference in The Hague from May 7–11 consists of 7 platform presentations and 24 poster presentations. The contributions cover results from investigations with a wide span of the organisms, compounds, environmental factors and methods employed in the NoMiracle project to fulfil the overall aim of developing and improving methods for combining human and environmental risk assessment. The tables below list the titles of the NoMiracle contributions and indicate where and when they are presented at the SETAC conference.

Abstracts are available on the SETAC and NoMiracle Internet Homepages:

<http://www.setac.org/>

<http://nomiracle.jrc.it/Documents/SETAC2006.doc>

## Platform presentations

Diffusive mass transfer of 12 PAHs at direct contact and through different exposure media	Tu 9/5 14:25–14:45	Mi	P01-NERI
Assessment of health risks in small areas	Mo 8/5 14:05–14:25	Ev	P03-UFZ
Harmonisation of extrapolation factors in human and ecological risk assessment	We 10/5 15:25–15:45	Eu	P04-RU
The effects of chronic exposure of the springtail <i>Folsomia candida</i> to soil polluted with a mixture of Chlorpyrifos and Nickel	Tu 9/5 8:30–8:50	Mi	P06-VU
An integrated genomics and proteomics approach for the detection of ecologically relevant biomarkers in <i>Daphnia magna</i>	Mo 8/5 12:05–12:25	Ev	P14-UA
A high resolution spatially explicit continental scale multimedia model of fate and transport of chemicals	Mo 8/5 8:30–8:50	Mi	P18-JRC
Risk Governance from cumulative stressors – a perspective from the social science	We 10/5 14:05–14:25	Vg	P32-DIA

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### Poster presentations

A novel method for measuring the chemical activity of PAHs in polluted soil	Tu 9/5 8:30–18:30	Mi	P01-NERI
Prioritisation and Precaution in Human and Ecological Risk Assessment	We 10/5 8:30–18:30	Eu	P01-NERI
Scenario selection in risk assessment – case of pharmaceuticals	We 10/5 8:30–18:30	Am	P01-NERI
Pro-inflammatory effects of chlorpyrifos and diazinon on human blood cells	Tu 9/5 8:30–18:30	Y1	P03-UFZ
Combined effects of mycotoxines on single cell organisms	Mo 8/5 8:30–11:30	Vg	P03-UFZ
Cumulative risk of nickel and chlorpyrifos on single cell organisms	Tu 9/5 8:30–18:30	Mi	P03-UFZ
The human cell line HepG2 as an in-vitro model for human risk assessment	We 10/5 8:30–18:30	Eu	P03-UFZ
Spatially explicit exposure modelling of ecological receptors in a heterogeneously contaminated floodplain	Tu 9/5 8:30–18:30	Kl	P04-RU
Estimating the toxic pressure of high production volume chemicals on remote ecosystems	Mo 8/5 8:30–18:30	Am	P04-RU
Understanding the dynamics of the toxicity of mixtures	Tu 9/5 8:30–18:30	Mi	P06-VU
Optimisation of exposure experiments	Th 11/5 8:30–11:30		P06-VU
Influence of nickel chloride, chlorpyrifos and binary mixtures of them on <i>Danio rerio</i> embryos and larvae	Th 11/5 8:30–11:30	Y1	P11-EKUT
A combination of gene expression data and biomarker endpoints to determine mixture toxicity of nickel and chlorpyrifos to the waterflea <i>Daphnia magna</i>	Mo 8/5 8:30–18:30	Vg	P14-UA
Pan-European Landscape parameters for multimedia fate and transport modeling of chemicals	Tu 9/5 8:30–8:50	Kl	P18-JRC
State-of-the-art in environmental risk mapping and visualization	Mo 8/5 8:30–11:30	Ev	P21-ALTERRA
Behavioural screening toxicity test for <i>Tubifex tubifex</i> (Oligochaeta)	Th 11/5 8:30–11:30	Kl	P24-LIMCO
Life cycle test of aquatic stages of <i>Chironomus riparius</i> exposed to Ni, Chlorpyrifos alone and in combination	Tu 9/5 8:30–18:30	Mi	P24-LIMCO
Effects of nickel chloride, chlorpyrifos and oxygen depletion on behaviour and vitality of zebrafish ( <i>Danio rerio</i> ) larvae	Th 11/5 8:30–11:30	Kl	P24-LIMCO P11-EKUT
Toxicity testing of various chemicals using the aquatic macrophyte <i>Lemna minor</i>	We 10/5 8:30–18:30	Y1	P25-RWTH
Biodegradation of Chemicals in Water-Sediment-Systems: A New Screening Tool	Th 11/5 8:30–11:30	Ev	P26-ECT
Cognitive neural networks analysis of organic pollutants persistence in the environment	Mo 8/5 8:30–8:50	Eu	P33-URV
Ensemble methods to enhance the identification of MOA's with deterministic and probabilistic network	Mo 8/5 8:30–18:30	Eu	P33 URV
Self-Organization of geostatistical information for vulnerability analysis – Does risk mapping and visualization help risk communication?	Mo 8/5 8:30–18:30	Ev	P33-URV
Modelling chemical multimedia partitioning with neural networks	Mo 8/5 8:30–18:30	Mi	P33-URV

## NoMiracle Newsletter No. 3

NOvel Methods for Integrated Risk Assessment of  
Cumulative stressors in Europe

### *First announcement of the*

#### **International School on Environmental Risk Assessment**

**Organised by Università degli Studi Di Siena**  
**Certosa di Pontignano**  
**Siena, Italy**  
**November 5-13, 2006**

The School is addressed to young scientists (PhD students, post-docs, and more experienced persons) interested in the field of ecotoxicology and environmental risk assessment.

It will be open to a maximum of 50 students.

Degrees in Biology, Natural and Environmental Sciences, Chemistry, Environmental Engineering will be preferred. Applications from students with a degree in related fields will be considered case-by-case.

#### **Preliminary list of lecturers**

Theo Brock (ALTERRA, The Netherlands)  
Antonio Di Guardo (University of Insubria, Italy)  
Antonio Finizio (University of Milano Bicocca, Italy)  
Cristina Fossi (University of Siena, Italy)  
Giada Frezzilli (University of Pisa, Italy)  
Bo Jansson (University of Stockholm, Sweden)  
Crispin Halsall (Lancaster University, UK)  
Joop Hermens (Utrecht University, The Netherlands)  
Claudio Leonzio (University of Siena, Italy)  
Stefano Loppi (University of Siena, Italy)  
Marcello Lotti (University of Padova, Italy)  
José Tarazona (INIA, Spain)  
Nico van Straalen (Vrije Universiteit of Amsterdam, The Netherlands)  
Marco Vighi (University of Milano Bicocca, Italy)

More information on the detailed programme and on the location can be found at the website of the School:  
[http://www.unisi.it/eventi/risk\\_assessment/](http://www.unisi.it/eventi/risk_assessment/)

Inscription Fee: € 1200

Fee includes: 7 days of lectures (more or less 6 hours per day), didactic material and complete accommodation (double room and meals) at the Certosa.

Deadline for registration: **September 15, 2006**.  
Online registration will be ready as soon as possible.

For any additional information not yet included at the website, please contact the Scientific Committee and the Organising Secretariat:

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Visit NoMiracle at: <http://www.nomiracle.jrc.it>

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\*Articles in the NoMiracle Newsletter do not necessarily reflect the attitude of the NoMiracle Newsletter.