June 2006

NoMiracle Newsletter No. 4

NOvel Methods for Integrated Risk Assessment of CumuLative stressors in Europe

NoMiracle Ph.D. program – courses offered 2006

Campus Groenenberger where the Ph.D. courses takes place.
Campus Groenenborger
(Green surroundings)

Main buildings:
Groenenborgerlaan 171 - BE-2020 Antwerp
By bus:
From station Antwerpen Berchem: line 21, 32
From Central Station: line 27, 32

Registration:
Applicants are requested to send applications to the NoMiracle Secretariat (NoMiracle@dmu.dk) and provide:

1. information about their own discipline and degree,
2. an abstract of half a page about their research and why they are interested in the course, and
3. a short CV including scientific education.

The deadline for registration is 15 August 2006. For more information on the courses please contact the teachers. After registration deadline more information will be send to those who have registered.

Members of the NoMiracle Consortium lead two Ph.D.-courses at the Joint ISEE/ISEA International Conference on Epidemiology and Exposure in Paris, 2-6 September, 2006. For more information and registration for the Paris courses please visit www.paris2006.afsset.fr

In 2006 five Ph.D.-shortcourses are offered by partners of the EU-FP6 integrated project NoMiracle. The courses will take place at the University of Antwerp, 11-12 September 2006 and addresses young scientists (Ph.D. students and young post-docs). In case of overbooking, Ph.D. students from the NoMiracle project will have first priority. The fee for Ph.D. students not working in the NoMiracle project is 150 € for a 1-day course and 75 € for a ½-day course.

NoMiracle scientific articles 2006

Harbers, J.V., Huijbregts, M.A.J., Posthuma, L., Van De Meent, D. 2006. Estimating the impact of high-production-volume chemicals on remote ecosystems by toxic pressure calculation. Environ. Sci. Technol. 40: 1573-1580.

Kühne, R., Ebert, R.-U., Schüürmann, G. 2006. Model selection based on structural similarity-method description and application to water solubility prediction. J. Chem. Inf. Model. 46: 636-641.

Reichenberg, F., Mayer, P. 2006. Two complementary sides of bioavailability: accessibility and chemical activity of organic contaminants in sediments and soil. Environmental Toxicology and Chemistry 25: 1239-1245.

NoMiracle Ph.D. courses in Antwerp September 2006

1. Framing Risk assessment

Duration	Date	Time	Room	Teachers	
1-day	11 & 12	9-17	U 241	**Dr. Peter B. Sørensen** **Dr. Marianne Thomsen**	pbs@dmu.dk mth@dmu.dk

To attend this course you will have to bring a laptop, with windows and at least 10 Gb free disk space. Excel will be an advantage.

2. Fate and Exposure Modelling

Duration	Date	Time	Room	Teachers	
1-day	12	9-17	US 103	**Dr. Ian Cousins** **Dr. Mark Huijbregts**	ian.cousins@itm.su.se m.huijbregts@science.ru.nl

3. Separation of uncertainty & variability in spreadsheet models

Duration	Date	Time	Room	Teachers	
1-day	11	9-17	US 103	Dr. Ad Ragas Drs. F. Brouwer	A.Ragas@science.ru.nl f.brouwer@science.ru.nl

4. Toxicogenomics

Duration	Date	Time	Room	Teachers	
½-day	11	9-13	US 213	**Prof. Wim de Coen**	Wim.DeCoen@ua.ac.be

5. Mixture toxicity: Response characterisation, Experimental design and Data analysis

Duration	Date	Time	Room	Teachers	
1-day	12	9-17	US 213	**Dr. Claus Svendsen**	csv@ceh.ac.uk

Dr. Peter B. Sørensen
Dr. Marianne Thomsen

Descriptions of courses

Course 1
Framing Risk Assessment

General
The identification of the scenarios for risk assessment is the governing factor for the final conclusion about the predicted risk level.

The student will learn about the scientific background for selection of the most relevant risk scenario. This includes a method to rank substances such as pesticides and biocides with respect to different criteria of toxicity and exposure. This way it is possible for instance to identify the most hazardous chemical or the five most hazardous chemicals in defined scenarios. This is important when the community prioritises its administration of hazardous chemicals.

The method ensures that chemicals are considered systematically and effectively with respect to potential harmfulness to human health and ecosystems. The method takes into account variables like scenario conditions and potential health effects.

Course objectives
After taking the course you will be able to:

- improve the scientific background of risk assessment using a scientific driven design of the governing conditions for subsequent detailed risk assessment
- combine a concept of criteria definition with a concept of multi-criteria analysis in order to perform a design of the most relevant conditions for more detailed risk assessment
- have a more complete picture of the uncertainty inherent in risk assessment.

Content
The selection of an appropriate scenario is a challenge in the case of risk evaluation and assessment for environment and human health. The demand of using several factors that may be quite complex induces a nearly infinite number of potential scenarios to be assessed that exceed any realistic limit of resources available for risk assessment.

A selection procedure is therefore needed in order to focus on the most relevant scenario. Selection of sub-optimal scenarios for risk assessment is a challenge for any selection procedure, because this will induce hidden uncertainty into the entire risk assessment procedure. Therefore, uncertainty management also needs to take into account the risk assessment scenario because this defines the circumstances for the risk assessment.

Consequently any relevant factor included in the assessment in principle needs to be addressed in the scenario selection procedure. The short course will elucidate the stepwise paradigm that is developed in the NoMiracle project (Novel Methods for Integrated Risk Assessment of Cumulative Stressors) as follows:

1. Defining the problem of risk assessment. Focusing the problem and related validity area (what is included and what is not included).

2. Define the governing set of criteria that are considered as essential for the specific risk assessment problem, here a structured criteria definition will be shown and used. A criterion in this context is not a data set, but a concept like e.g. "Bioaccumulation". In this step it is important not to ignore important criteria and expose too much attention to less important, thus inducing a bias into the analysis.

3. Estimate the criteria using existing data sets to form criteria data and evaluate the associated uncertainty. At this step the criteria data become estimators for the criteria and it may turn out that there are data gaps where a criterion is not covered by any existing criterion data. Two types of uncertainty are involved at this stage:
(1) Goodness of fit between criteria data values and criteria as phenomenon.
(2) The criteria data value uncertainty.

   The criteria data values defines the real set of scenarios that are candidates for being the most relevant for risk assessment.

4. The third step is to relate the single criterion data value to each other in a multi-criteria analysis for selection of scenarios. The problem of conflicting data sets for different criteria will induce uncertainty into the finding of the most relevant scenario.

   A multi-criterion method based on partial order theory will be described and used. Application of criteria data set in multi-criteria ranking with respect to the identification of the worst case scenario for risk assessment. The main principle in multi-criteria analysis methods will be briefly described. Focus will be on the use of a stochastic principle in the multi-criteria analysis as based on Partial Order Theory paradigm for operational ranking following the concept of linear extension as described in Davey and Priestly, 1990. The approach is made practicably useable by Sørensen et al. 2000, and Lerche et al., 2003 and is now in a stage where it is possible for non-experts in ranking theory to do the application on real problems using the free-ware RangProp. The application in relation to risk assessment of chemicals is discussed by e.g. Sørensen et al., (2005).

Every participant has to bring a lab-top computer using Windows (installation of a simple exe file will take place).

References

Davey, B.A., Priestly, H.A. 1990. Introduction to Lattice and Order, Cambridge University Press, Cambridge UK.

Sørensen, P.B., Lerche, D. and Brüggemann, R. 2005. Resources and uncertainties in evaluation of chemicals, Water Science and Technology, Vol. 52, No. 6, pp. 235-242.

Sørensen, P.B., Lerche, D., Carlsen, L. and Brüggemann, R. 2001. Statistically approach for estimating the total set of linear orders – A possible way for analysing larger partial order set -. Berichte des IGB, Heft 14, Leibniz-Institute of freshwater ecology and inland fisheries, Forchungsverbund berlin e.V.

Lerche, D., Sørensen, P., Brüggemann, R. 2003. Improved Estimation of Ranking Probabilities in Partial Orders using Random Linear Extensions by Approximation of the Mutual Ranking Probability, J. Chem. Inf. Comput. Sci, Vol. 43, pp. 1471-1480.

Dr. Ad Ragas

Course 2
Fate and Exposure Modelling

General
You, the student, will learn about the different modelling approaches currently used in the research field of environmental chemistry, as well as in risk assessment and regulation perspectives (e.g. the EUSES modelling tool). You will learn to apply models to investigate, understand and generalize how physical-chemical properties govern the environmental fate and wildlife exposure to organic substances.

Course objectives
After taking this course you are expected to be able:

- **to identify problems or contexts in the field of environmental chemical research where model simulations can enhance the process understanding,**
- apply models to predict chemical fate and exposure,
- **to identify and qualitatively understand differences in the environmental fate and the exposure of wildlife and humans to different classes of chemicals,**
- **to interpret and reflect over simulation results and the impact of different parameters on the model outcome,**
- to critically evaluate the application of different modeling approaches in environmental chemistry.

Course content
- Transport and distribution processes and reactions of non-polar and polar organic compounds
- Basic modeling concepts of particular applicability for environmental chemistry
- Multi-media environmental fate models
- Exposure models: external and internal exposure of wildlife and humans
- Food chain models: bioaccumulation and biomagnification
- Sensitivity and uncertainty analysis in modeling.

Teaching methods
The course will comprise a combination of lectures and computer workshops in which hands-on experience will be gained in using various modelling tools and solving problems.

Course 3
Separation of uncertainty & variability in spreadsheet models

General
This course is intended for Ph.D students from research areas adjoining to exposure assessment, who are interested in these assessments and are willing to learn more about the application of probabilistic risk assessment methods in this field.

Course objectives
After taking the course you will be able to transfer theoretical knowledge about uncertainty and variability and to train the practical skills involved. Problems arising when applying the techniques for the separation of uncertainty and variability will be addressed.

Content
Each individual within a population has its own characteristic activity and dietary pattern and its own physiological parameters, which in addition may vary in time.

These differences lead to variability in exposure and effect between individuals. Variability can be defined as the temporal, spatial or intersubject differences in the value of a certain parameter.

Parameters can also be uncertain, which can be thought of as a measure of the incompleteness of one's knowledge (Cullen & Frey, 1999). Theoretically, uncertainty can be eliminated by gathering more information, in contrast to variability, which is inherent in the system and cannot be eliminated by doing additional research (Decisioneering, 2000).

Variability and uncertainty are, as explained above, two different characteristics of a system. Because variability and uncertainty can have different implications for decision making, it may be useful to consider them separately in an analysis.

This course will focus on the separation of variability and uncertainty in NORMTOX.

This is an integrated human exposure model. It predicts the lifetime-averaged daily intake of a contaminant and compares it with the acceptable daily intake (Ragas & Huijbregts, 1998). Results are reported as frequency charts, in which variance originates from interindividual variation (e.g. body weight and consumption patterns) and from a lack of knowledge (e.g. the true value of oral or inhalatory absorption fractions).

Because this dual origin of the variance impedes an unequivocal interpretation of the model outcome, it should be separated and visualized individually.

This separation of interindividual variability and uncertainty can be established by combining ANOVA techniques and a second order Monte Carlo simulation. Analysis of Variance (ANOVA) techniques are used to separate different sources of uncertainty in the input files, and to quantify the contribution to the total uncertainty and variability.

The influence of true uncertainty in the risk predictions of NORMTOX are separated from the influence of interindividual variability by means of nested Monte Carlo simulation. This technique propagates the different sources of uncertainty through the model. Results can therefore be presented as the population fraction at risk, due to interindividual variability in consumption and activity patterns, and the probability of this risk.

The training course is conducted in the framework of the integrated project NoMiracle (Novel Methods for Integrated Risk Assessment of Cumulative Stressors in Europe) of the European Sixth Framework Programme "Global Change and Ecosystems".

Format and time

To get insight in the problematic nature of the matter, NORMTOX can be brought as a case study in which the attendants build up the model themselves.

To come to solutions for the upcoming problems this case study will be introduced and guided by several lectures in which the requisite techniques are explained. The course is best scheduled during a whole day, which will consist of approximately 2 hours of lectures in total and 6 hours case study with practical skills training. During the case study Crystal Ball and Excel will be utilized, therefore the location must have computers provided with this software or the possibility to install this software.

References

Cullen, A.C., Frey, H.C. 1999. Probabilistic techniques in exposure assessment, A handbook for dealing with variability and uncertainty in models and inputs. Society for Risk Analysis, Plenum Press, New York.

Decisioneering, 1988-2000. Crystal Ball 2000, User Manual (pp 299). Decisioneering, Inc, Colorado, USA.

Ragas, A.M.J., Huijbregts, M.A.J. 1998. Evaluating the coherence between environmental quality objectives and the acceptable or tolerable daily intake. Regulatory Toxicology and Pharmacology 27, 251-64.

Course 4
Toxicogenomics

Prof.
Wim de Coen

Content

Toxicogenomics is a scientific subdiscipline that combines toxicology (the study of the nature and effects of poisons) with genomics (the investigation of the way that our genetic make-up, the genome, translates into biological functions). It has come into being only in the past couple of years. It has been made possible through an investigative technique using microarrays (also called DNA chips), which contain many hundreds or thousands of short DNA strands, each in its own compartment. By washing a solution of a substance over the whole chip at once, the section of DNA affected can be made to fluoresce, so indicating which genes are turned on by the substance and so suggesting its likely effect on the body (in the jargon of the business, taken from computing, the chips are *massively parallel* discovery processes).

It may soon be possible to include the whole human genome on such a chip and so test all of it at once for possible adverse effects (www.worldwidewords.org).

No further description available at present. For further information please contact the course responsible Prof. Wim de Coen.

Course 5

Mixture toxicity: Response characterisation, Experimental design and Data analysis

General

This course will be teaching the basic concepts of mixture toxicity analysis, and build this to an understanding of what lies behind the more detailed analysis of mixture effect patterns that we analyse using the MIXTOX model within NoMiracle. You will learn how to use this model for analysing mixture data and what experimental design issues are important to consider before starting your mixture experiments.

Course objectives

After taking this course you are expected to:

- understand the different ways normally used to analyze mixture data
- understand and use the MIXTOX model for data analysis,
- interpret and reflect over what different effect patterns might mean is going on,
- critically evaluate existing data sets and design experiments to avoid data being "overanalyzed".

Course content

- Basic concepts of concentration addition (CA) and independent action (IA)
- Toxic unit concept
- The biologically relevant deviations from of CA and IA
- Ways to analyze and depict mixture data
- The MIXTOX model (theory & practical PC work)
- Experimental design: How to ensure the experiments can address your question?

Teaching methods

The course will comprise a combination of lectures and computer workshops in which hands-on experience will be gained in using various modelling tools and solving problems.

References

Jonker, M.J., Svendsen, C., Bedaux, J.J.M., Bongers, M and Kammenga, J.E. 2005. Significance testing of synergistic/antagonistic, dose level–dependent, or dose ratio–dependent effects in mixture dose–response analysis. Environmental Toxicology and Chemistry, 24, 2701-2713. Also see: http://www.ceh.ac.uk/sections/er/csvendsen.html

NoMiracle co-ordination

Visit NoMiracle at: http://nomiracle.jrc.it

For further information contact

NoMiracle Secretariat
E-mail: nomiracle@dmu.dk

- Project co-ordinator and Editor responsible under the press law*:
  Dr. Hans Løkke
  National Environmental Research Institute,
  Vejlsøvej 25, P.O. Box 314,
  DK-8600 Silkeborg, Denmark
  Phone +45 8920 1482
  Fax +45 8920 1414
  E-mail: hlo@dmu.dk

- Databases and selection of scenarios:
  Dr. Hanne Bach
  National Environmental Research Institute, Denmark
  E-mail: hba@dmu.dk

- Exposure assessment:
  Professor Gerrit Schüürmann
  UFZ, Umweltforschungszentrum Leipzig, Germany
  E-mail: gerrit.schuurmann@ufz.de

- Effects assessment:
  Dr. Dave Spurgeon
  NERC, Centre for Ecology and Hydrology, United Kingdom
  E-mail: dasp@ceh.ac.uk

- Risk Assessment:
  Dr. Ad Ragas
  Radboud Universiteit Nijmegen,
  The Netherlands.
  E-mail: A.Ragas@science.ru.nl

Subscription on NoMiracle Newsletter:
send an e-mail to NoMiracle@dmu.dk

The integrated project NoMiracle
is funded by the European Commissions
Sixth Framework Programme.

EC Scientific Officer for the project:
Dr. Jürgen Büsing.