



# OSIRIS Newsletter

No. 3

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Photos: Andrea Kihlberg

## Second OSIRIS Annual Meeting



OSIRIS Annual Meeting 2009

Photo: Fotostudio Van Galen, Odijk, The Netherlands

## Second OSIRIS Annual Meeting

16–18 March 2009 • RIVM, Bilthoven, The Netherlands



### Meeting at RIVM in Bilthoven

The Second OSIRIS Annual Meeting took place on 16-18 March 2009 at the National Institute for Public Health and the Environment (RIVM) in Bilthoven, The Netherlands.

2009 is the 100 year anniversary of RIVM, which was therefore pleased to host the OSIRIS meeting on this special occasion. Alternative methods and the 3 R's are important subjects for RIVM.

76 participants from 14 countries and 29 OSIRIS partner institutes as well as from the Advisory Board met to discuss the results of the second project year and the further planning.

### Results achieved in the second project year

On the first day, partners from the five Research Pillars – Chemical Domain, Biological Domain, Exposure, Integration Strategies and Tools,



Case Studies – presented the major results achieved. This included among others:

In **Pillar 1**, the current edition of the software package ChemProp includes data-related structure searching, tautomer handling, application of qualitative and quantitative structure-activity relationships (QSARs) for physico-chemical and ecotoxicological endpoints, and a state-of-the-art tool to address the physico-chemical and structural domain of QSAR models.

Screening criteria for substance specific waiving of bioassays have been developed, i.e. a decision tree to identify non-bioaccumulative compounds based on trigger values for certain partition coefficients.

The developed software module for the determination of applicability domains of QSAR models was presented.

In **Pillar 2**, databases covering various endpoints, ranging from mutagenicity, carcinogenicity and repeated dose toxicity to reproductive toxicity, have been developed and newly collected data has been included, e.g. toxicity data made available from Russian language sources.

For the optimisation of *in vivo* testing strategies, existing *in vivo* ecotoxicity data has been evaluated (without performing *in vivo* testing).

Results of the MOA Workshop (held October 2008 in Liverpool, UK) discussions on how to use modes of action and mechanisms of action in an Integrated Testing Strategy (ITS), as well as first results of an interspecies comparison of toxicity tests (*in vitro* and omics data) were presented.

### Second OSIRIS Annual Meeting



In **Pillar 3**, further analysis of exposure assessment models has been carried out. A particular focus was on identifying “no-further-action levels”, and on the impact of variability and model scenario uncertainty on conclusions that lead to either waiving or triggering of tests in an ITS.

A bioaccumulation model, regional models for ionisable compounds and for parent compounds and transformation products, as well as a model for the estimation of the bioconcentration factor for ionisable compounds have been developed.

The initial PBPK (physiologically based pharmacokinetics) method development for prediction of distribution and elimination was based on data for pharmaceutical compounds, because of the lack of available data for industrial compounds.

In **Pillar 4**, a method for cost-effectiveness analysis as decision aid for test selection in the REACH context has been developed.

A guidance on the allocation of weight factors in a quantitative Weight of Evidence (qWoE) approach has addressed information needs, test validity, and data quality issues. Bayesian networks allow to express the reliability of a conclusion based on multiple information sources in terms of a (posterior) probability.

An ITS flow chart for fish toxicity has been developed, covering classification and labelling (C&L), PBT (persistent, bioaccumulative, toxic) assessment, and chemical safety assessment.

The current version of the OSIRIS web tool includes preliminary ITS versions for bioconcentration and mutagenicity. IUCLID5 files with test data can be imported, and a help system and user management functions are available. The

web tool will later be made available to stakeholders from industry and regulatory authorities.

In **Pillar 5**, two scenarios (experimental vs. estimated properties) were studied with regard to PBT labelling in order to evaluate the dependence of the outcome on the type of input data used.

The quality of CMR (carcinogenic, mutagenic, reprotoxic) screening through currently available *in silico* tools has been assessed.

Threshold of toxicological concern (TTC) values for drinking water have been derived from those for food additives by setting an allocation of 10% from the total daily intake to exposure from tapwater, assuming an intake of 2 L/day.

In the context of research into TTC for the workplace, methods to predict lung retention and nasal pungency thresholds (NPT) of organic vapours have been explored.

**Work package 6** (Training) reported on the planned programme for the second ITS training course, scheduled to be held in September 2009 in Milan, Italy. It will comprise both lectures on basic concepts underlying risk assessment and the REACH regulatory framework and practical demonstrations.



## Second OSIRIS Annual Meeting



### Stakeholder feedback

One plenary session was dedicated to the presentation and discussion of feedback on the project received from stakeholders.

A summary of the discussions at the Second OSIRIS Stakeholder Workshop on 17 November 2008 in Brussels, Belgium, was given, and comments received from the Advisory Board were presented. For instance it was called for a transparency of the models, ITS and weight of evidence approaches developed; for an availability of the web tool and data in time and further maintenance in the future; for the acceptance of the ITS by ECHA and non-European authorities.

### Intra- and inter-Pillar discussions

Several Pillar break-out sessions were scheduled to allow intense discussions within the Pillars of the results achieved in the second year as well as of the further planning of the project.

Moreover, a plenary session was dedicated to inter-Pillar interactions in order to identify information needs within Pillars and work packages and to coordinate the activities in the next project year.

### Further planning of the project

The new objectives, deliverables and milestones set in the individual Pillars for the next 18 project months were presented in the plenum and cross-Pillar interactions were discussed. A timeline for the future activities and interactions within work packages, across work packages and across Pillars was set.

### Working group meetings and workshop

During the Annual Meeting several inter-Pillar working groups met for face-to-face discussions, e.g. on the bioconcentration factor ITS and on data quality.

One focus of the OSIRIS project is the analysis of uncertainties. This issue is addressed throughout all Pillars and is an important factor of the ITS developed. Therefore an extra workshop on uncertainty analysis in ITS, organised by Pillars 3 and 4, took place subsequent to the Annual Meeting.

### ...last but not least

The convivial evening with an Indonesian buffet sponsored by RIVM and the sunny spring weather contributed to the success of this Second Annual OSIRIS Meeting.



Photos: Sonja Jansen, Andrea Rühoff

### OSIRIS Partners



#### Technical University of Denmark– DTU (Partner 6)

Department of Environmental Engineering  
Ecotoxicology and Environmental Chemistry Research Group  
Lyngby, Denmark

WP 3.1 leader, Deputy Pillar 3 Co-ordinator

The Department of Environmental Engineering (ENV) is a department at the Technical University of Denmark (DTU) aiming at developing technical and sustainable solutions to minimise the impact of society on the environment through research and teaching in water supply, waste water, solid waste, hydrology, geology, ecotoxicology, environmental chemistry and microbiology at an international level.

DTU ENV is one of the largest university groups specialising in environment and resources in Europe. The researchers at DTU ENV are drawn from the best universities in more than 15 different countries. The department has obtained the Stockholm Water prize and the Heineken award, among others.

#### The Ecotoxicology and Environmental Chemistry Research Group:

The Ecotoxicology and Environmental Chemistry research group is concerned with the impact and



Photo: Julie Camilla Middleton

fate of chemicals and nanomaterials in the environment, and the development of the tools required for environmental risk assessment of chemicals.

Within OSIRIS, DTU has the task to develop modern tools for the evaluation of indirect exposure of humans and wildlife via the environment. Currently, the focus is on bioaccumulation models, on exposure models for ionisable compounds and on the uncertainty of estimates.



#### Istituto di Ricerche Farmacologiche "Mario Negri"– IRFMN (Partner 8)

Laboratory Environmental Chemistry and Toxicology  
Milan, Italy

WP 4.3 leader, Deputy Pillar 4 and Training Activities  
Cross-cutting Co-ordinator

The Mario Negri Institute for Pharmacological Research is the first Italian not-for-profit foundation entirely dedicated to — mainly bio-medical — research and education. It is a private Institute but works for the public interest, being completely independent of industry, universities and the state. It is free from political pressure and boasts the efficiency of a private organisation, taking the approach of "private enterprise serving the public interest". Dissemination, training and public availability of the results are pursued, no patents are taken out.

The Institute comprises almost 900 staff members in four locations in Italy: Milan, Bergamo, Ranica and Santa Maria Imbaro.

**Laboratory Environmental Chemistry and Toxicology:** The Laboratory of Environmental



Photo: Andrea Richarz

Chemistry and Toxicology belongs to the Department of Environmental Health Sciences whose focus is the analysis of environmental factors and their effects on human health.

The Laboratory is mainly involved in the development of predictive toxicology models (QSAR) for REACH relevant compounds, pesticides, endocrine disruptors, studies on environmental toxicological and ecotoxicological properties of chemicals, risk assessment of pollutants, and environmental monitoring.

### OSIRIS Partners



#### Bourgas University "Prof. As. Zlatarov" – LMC (Partner 22)

Laboratory of Mathematical Chemistry  
Bourgas, Bulgaria



Photo: LMC homepage

WP 1.3 leader, Deputy Cross-cutting Co-ordinator of Modelling Work

The Laboratory of Mathematical Chemistry was founded in 1983 as a Laboratory for Structure Activity (property) Modelling. LMC comprises researchers from different disciplines: chemists, physicists, programmers and mathematicians. LMC has bilateral cooperation and research contracts with major industrial companies (Procter&Gamble, 3M, Exxon Mobil, Astra Zeneca, Du Pont, BASF, L'Oréal, Givaudan, Unilever), state agencies (German, Australian, Canadian, US, Danish EPA; Health Canada; Japanese NITE, NIHS and NIES) and international regulatory institutions (European Chemicals Agency (ECHA), OECD, Joint Research Centre of the European Commission).

#### LMC Research Focus:

LMC research focuses on (quantitative) structure activity relationship ((Q)SAR) modelling of ecological and human health endpoints,

database building and *in silico* simulation of metabolism and catabolism:

- IT for structure complexity evaluation (conformer flexibility and metabolic transformations)
- Assessing molecular reactivity and interaction mechanisms
- Mechanistically transparent QSAR models
- Simulating environmental and tissue metabolism
- Modelling toxic effects resulting from metabolic activation of chemicals
- Evaluating model applicability domains
- Selecting chemicals for strategic testing
- 3D databases.



#### Istituto Superiore di Sanità – ISS (Partner 11)

Department of Environment and Primary Prevention  
Rome, Italy



Photo: Photographic archive of the Istituto Superiore di Sanità

The Istituto Superiore di Sanità (ISS) is the leading technical and scientific public body of the Italian National Health Service. Its activities include research, control, training and consultation in the interest of public health protection. The Institute conducts scientific research in a wide variety of fields, from cutting-edge molecular and genetic research to population-based studies of risk factors for disease and disability.

#### The Department of Environment and Primary Prevention:

The Department combines chemical, toxicological, biological, microbiological and epidemiological expertise in qualitative and quantitative risk assessment. It defines guidelines for environmental (bio)monitoring programmes and proposes preventive measures for risk management and reduction.

Scientific activities include studies on exposure

to chemical, physical and biological agents and their effects on human health and the environment. Special consideration is given to: persistent toxic pollutants (e.g. PAHs, dioxins, PCBs, flame retardants); plant protection products/residues; biocides; cosmetics; metals; powders, fibres; natural toxins; endocrine, mutagenic and carcinogenic substances; materials in contact with food and drinking water; toys; waste; water quality. Research on toxicity mechanisms – using advanced techniques, alternative methods, chemobiokinetic studies and the identification of biomarkers – aims at characterising health risks in the population.

### OSIRIS Partners



#### Vrije Universiteit Amsterdam – VU (Partner 13)

Department of Animal Ecology  
Amsterdam, The Netherlands

The Department of Animal Ecology is part of the Institute of Ecological Sciences and belongs to the Faculty of Earth and Life Sciences of the Vrije Universiteit (VU) Amsterdam.

It investigates the intriguing diversity of animal life and its adaptation to environmental change, studying responses to stress on the molecular, population and community level. It also works on the development of instruments for the assessment of possible ecosystem effects of soil pollution. Furthermore, the research aims at establishing a relationship between effects of toxicants at the individual level and the response of populations and ecosystems.

#### The Ecotoxicology Section:

In the Ecotoxicology Section of the Department, research focuses on the analysis of the response of soil invertebrates to toxicants in soil.



*Photo: VU University Amsterdam homepage*

Research involves the study of bioavailability and uptake routes, internal distribution and effects of toxicants in these organisms and the relation between internal concentrations and effects. Mechanisms of adaptation to toxicant stress are studied in soil invertebrates, and molecular biology tools (genomics) are used. The results of the ecotoxicological studies and biomarker tests are aimed for the risk assessment of chemicals in the environment.



#### SIMPPLÉ S.L. – SIMPPLÉ (Partner 14)

Research and Development  
Tarragona, Spain

WP 4.4 leader

SIMPPLÉ is an SME focused on technological innovation in the field of chemical engineering, eco-innovation and computer science, located in Tarragona, Catalonia.

Its department of System and Software Engineering possesses a large expertise in the field of artificial intelligence, predictive analysis, machine learning and data mining techniques as well as a demonstrated experience in the management and development of scientific software projects.

#### The Research and Development Team:

Research and development efforts focus on the application of the team's experience in machine learning, predictive analysis and data mining techniques to new fields.

The R&D team has developed novel systems for



*Photo: Patronat Municipal de Turisme de Tarragona*

indexing and searching information on the internet or intranets. Network analysis methods borrowed from physics have been applied to the assessment of social networks in organisations, providing managers with a powerful tool to assess the social capital of the organisation.

In the risk assessment of chemicals, the R&D team develops software tools to integrate and evaluate information from several sources, providing the user with a clear guidance to make informed decisions in a transparent and straightforward manner.

### OSIRIS Partners



#### KWR, Watercycle Research Institute – KWR (Partner 15)

Chemical Water Quality Team  
Nieuwegein, The Netherlands

WP 5.4 leader

With its extensive history in drinking water research and its sights set on current and future water problems, KWR (previously Kiwa Water Research) has extended its field of activities to include the entire watercycle. KWR helps the water sector to identify the challenges it faces, and offers the means and innovative strategies to meet them successfully.

Thanks to its extensive national and international knowledge networks and its research and developments, KWR acts as bridge-builder between science, business and society, making top knowledge available to the whole water sector.

#### The Chemical Water Quality Team:

Changes in society and in natural conditions have an impact on the quality of drinking water sources. Developments are necessary in the regulatory frameworks, including the Water Framework Directive, the New Groundwater



Photo: KWR

Directive, REACH, the EU Drinking Water Directive and the New Drinking Water Decree.

The Chemical Water Quality team assesses current and future chemical and toxicological water quality issues. It focuses on investigating the presence, behaviour and effects of chemical pollution in watery environments, and the possible consequences for the provision of (drinking) water.

Advanced analytical methods (analytic-chemical, toxicological *in vitro* tests and sensing) are developed, monitoring is conducted, and health-based assessments are provided.



#### Institute of Public Health of the Republic of Slovenia – IVZRS (Partner 16)

Department of Toxicology  
Ljubljana, Slovenia

The Institute of Public Health of the Republic of Slovenia (IVZRS) is a national institute founded in December 1992 by the Decree of the Government of the Republic of Slovenia to cover the areas of Social Medicine, Hygiene, Environmental Health, Epidemiology, Informatics and Research activity. The Institute's most important activities are to perform and implement the national programme of preventive medicine, to collect and analyse data about the health of the population and health-care services and, on the basis of reliable data, to prepare documents for healthcare policies.

#### The Department of Toxicology:

The Department of Toxicology aims at assuring and promoting chemical safety. The main tasks include risk assessment for human health, public health aspects of toxicovigilance, research, and teaching. Its role in the national registration



Photo: Sonja Jeram

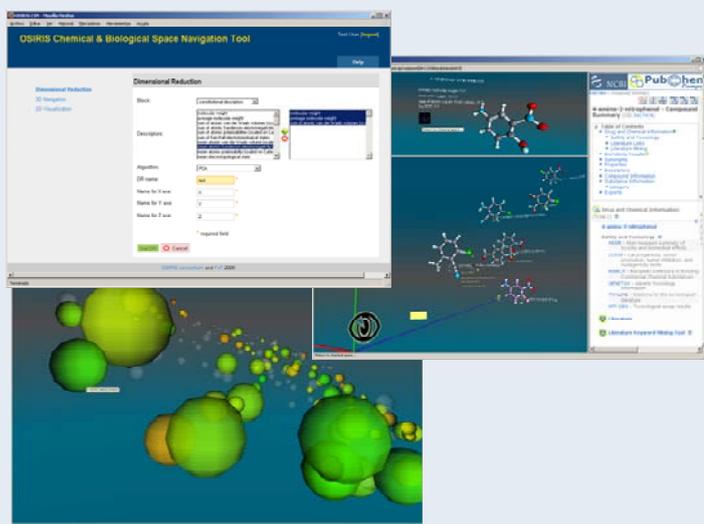
procedure of plant protection products includes toxicological hazard assessment, risk assessment for operators, workers and bystanders, and assessment of toxicological information, first aid and treatment advice supplied with individual preparations.

Department members review draft assessment reports for inclusion of active substances in Annex I of Directive 91/414/EEC and regularly attend Pesticide Risk Assessment Peer Review meetings at the European Food Safety Authority.

## OSIRIS Results Highlights

### OSIRIS Chemical & Biological Space Navigation Tool (Partner URV)

Universitat Rovira i Virgili, Transport Phenomena research team, Tarragona, Catalonia, Spain



The development of an automated system to implement intelligent testing strategies requires the analysis of a huge amount of chemical and biological data with the purpose of establishing cause and effect relationships or to infer unknown properties based on molecular similarity principles.

The OSIRIS Chemical and Biological Space Navigation Tool is conceived as a visual aid for pre-screening tasks and is designed to facilitate the exploration of the relationships between chemical structure, physico-chemical properties and environmental endpoints.

The current prototype incorporates a set of basic data analysis functionalities (dimension reduction and data clustering) coupled with a 3D interactive graphic engine. The interactive navigation capabilities of the application can be used to develop a virtual platform for visual screening of chemicals in the context of the REACH regulation. The prototype tool also includes a first approach to 2D cartographic visualization using Self-Organizing maps and the Google Maps application programming interface to provide basic GIS capabilities.

The first version of the navigation tool has been implemented as a web-based application and is accessible on-line from the OSIRIS intranet for the OSIRIS Consortium.

### Database functionality for tautomers (Partner UFZ)

Helmholtz Centre for Environmental Research—UFZ, Dep. of Ecological Chemistry, Leipzig, Germany

Storing chemical structure information in databases relies on the unique and unambiguous computerisation of the chemical structure. Disregarding the constitutional and conformer differences as reflected in 3D coordinates, a database entry is supposed to be unambiguous by storing the compound's connection table, i.e. characterising a molecule by listing all atom types and bonds/bond grades between them.

However, this is only true for fixed configurations, whereas in reality tautomerism occurs for many compounds. Tautomer relocations are caused mostly by moving hydrogen atoms and bond grades for involved atoms changing accordingly. The relocation process is very fast, and the equilibrium balance often depends on environmental conditions. Thus tautomerism is not considered as chemical reaction, but sets of tautomers are treated as same compounds.

Without addressing tautomerism the database storage of chemical structures is arbitrary. An algorithm to identify tautomers is required, allowing matches with the structure in the database for any tautomer form of a given molecule, and retrieval of tautomers from the database, without storing all individual forms.

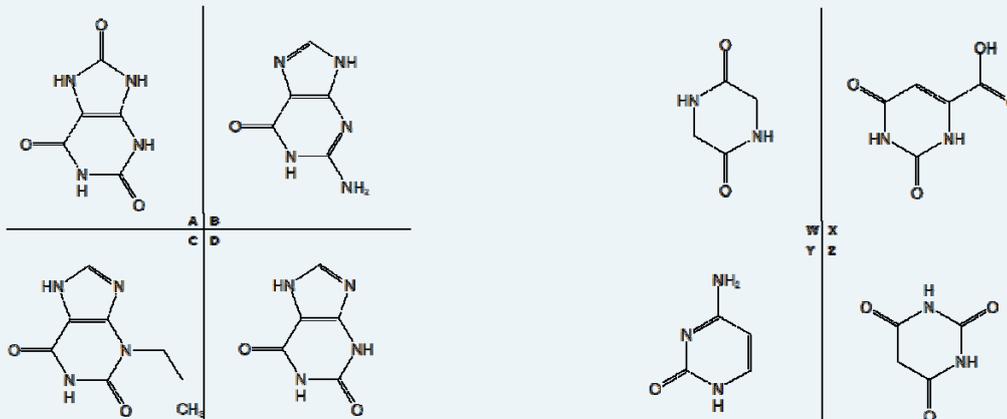
The comparison of two molecules with respect to tautomerism has been addressed, and an algorithm to use InChI layers for tautomer generation has been developed and implemented in the OSIRIS database.

The importance of tautomer distinction has been demonstrated by model calculations for a large data set of ca. 70000 compounds: For about 12% of these chemicals, tautomerism has been observed based on InChI code. Example calculations for the soil sorption coefficient and for water solubility have yielded significantly different results for sets of tautomers.

## OSIRIS Results Highlights

QUIZ

Solution on page 12.



Which structure(s) has (have) the most tautomers?

Which structure(s) has (have) 6 tautomers?

Additional information: The relevant acceptors were selected by InChI. Only heteroatoms can serve as H acceptor or donor.

## Database on (eco)toxicity data available from Russian language sources

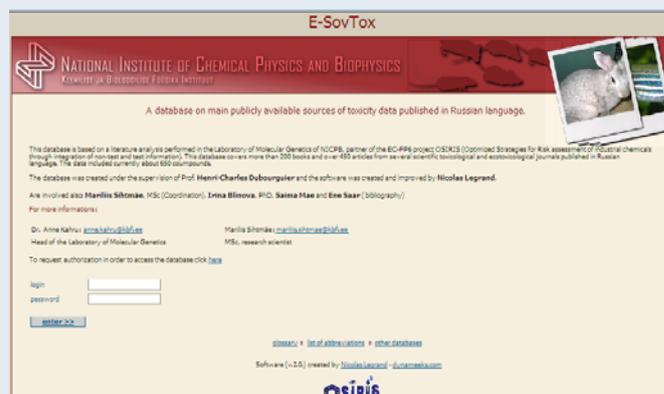
(Partner NICPB) National Institute of Chemical Physics and Biophysics, In vitro &amp; ecotoxicology group, Tallinn, Estonia

Toxicity data are collated for the development of (quantitative) structure-activity relationships and integrated testing strategies. A novel aspect of data collection has been the searching of literature published in Russian in the former Soviet Union and Russia. The search performed in Estonian and Russian libraries and on websites covered books, journal articles, electronic databases and PhD dissertations.

The web-database E-SovTox including eco- and toxicological data has been created using php and SQL. The database contains not only numerical data but also literature references and abstracts in two languages (Russian and English) as well as original documents as pdf files. The search engine can be used both with Roman and Cyrillic characters.

In the database, each compound is presented on a separate page including:

- General information (CAS no, molecular weight, synonyms, common usage)
- Direct access to extended search engines
- Mammalian toxicological / ecotoxicological data
- Comments, references etc.



Toxicological data originate mainly from the Russian journal "Industrial Hygiene and Occupational Diseases" (Гигиена труда и профессиональные заболевания), ecotoxicological data from the Russian journals "Hydrobiological Journal" (Гидробиологический журнал) and "Inland Water Biology" (Биология внутренних вод).

Altogether ~490 articles and ~650 substances with toxicological data and 44 ecotoxicological papers and 42 compounds are currently included in the database.

The database will be improved and terms of use defined. Its public opening is planned in 2010.

**Additional information:**

Sihtmäe M, Dubourguier HC, Kahru A 2009. Toxicological information on chemicals published in the Russian language: contribution to REACH and 3Rs. Toxicology, in press

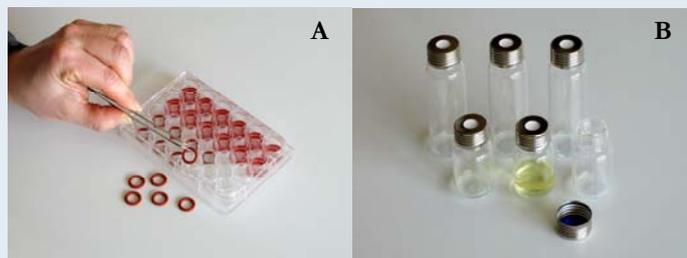
## OSIRIS Results Highlights

### Passive dosing to control (semi)volatile substances (Partner AU-NERI)

Aarhus Universitet – NERI, Dep. Environmental Chemistry and Microbiology, Roskilde, Denmark

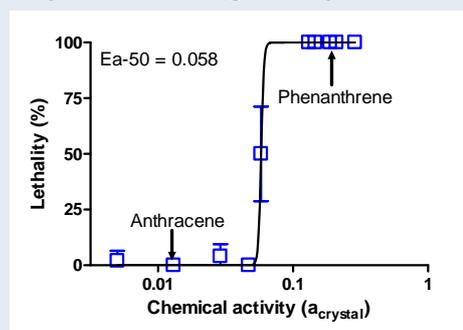
Many toxicity test systems are prone to evaporative and sorptive losses of hydrophobic organic compounds (HOCs), compromising the validity and applicability of the test results. Passive dosing by equilibrium partitioning from a polymer is a strategy to establish and maintain constant and well defined HOC test exposure levels. The HOC is provided by partitioning from a dominating polymeric phase, rather than by adding it via a solvent extract. Advantages include controlled and constant freely dissolved concentrations (or chemical activity), and that organisms are not co-exposed to solvents.

Silicone has been selected as the optimal polymer, and its compatibility with different test organisms tested and confirmed. HOC loading



Passive dosing with silicone O-rings in 24 well plates (A) and in glass vials with cast silicone in the bottom (B).

into the polymer and release kinetics into the test medium have been systematically investigated for various passive dosing formats. Equilibrium freely dissolved concentrations are rapidly reached, and maintained for the test duration. Passive dosing is currently being applied successfully in a range of invertebrate and *in vitro* toxicity assays. As an example, the limit toxicity (= at solubility) of 10 polycyclic aromatic hydrocarbon (PAH) compounds to the springtail *Folsomia candida* has been determined using the passive dosing vials pictured.



Lethality of the springtail *F. candida* after 7 days exposure to 10 PAHs plotted against the chemical activity of the PAHs. Lethalities (mean  $\pm$  stdev) of all PAHs were fitted to one uphill function (Mayer P and Holmstrup M 2008. Environ Sci and Technol 42: 7516–7521).

### Recommendations for updating EUSES (Partner RIVM)

RIVM, Expertise Centre for Substances, Bilthoven, The Netherlands

REACH integrates the concept of exposure informed testing as part of the overall risk assessment process. Depending on the exposure – which is different for each identified use – some tests may be waived (Exposure Based Waiving), while others may be triggered (Exposure Based Triggering). To support the decision-making process based on exposure information, good criteria, tools/methods, and consequent guidance need to be available.

Within OSIRIS Pillar 3 (Exposure), a first set of recommendations have been made for updating the European Union System for the Evaluation of Substances (EUSES) as part of the chemical safety assessment methodologies under REACH.

The current insights on exposure assessment performance can also be used for updating the current REACH guidance documents.

The recommendations are supporting ongoing developments in Pillar 4, being the incorporation of an Exposure Based Waiving/Threshold of Toxicological Concern module as part of the intended OSIRIS integrated testing strategy.

They concern environmental exposure and hazard assessment and are split into two levels requiring different degrees of additional refinement before implementation.

The recommendations comprise:

- the updating of environmental exposure models with a refined local model for bio-

### OSIRIS Results Highlights

- accumulation, a regional model incorporating calculations on environmental concentrations and related degradation products, a multimedia regional model for neutral and ionisable organic compounds, and a new root model
- the integration of uncertainty analysis into

chemical safety assessment tools such as EUSES

- recommendations on how future assessments should provide better insight into the uncertainty of the various parts of the exposure assessment, such as emission factors, models and parameters, scenarios, etc.

### Regional dynamic model for ionisable compounds (electrolytes) (Partner DTU)

DTU Ecotoxicology and Environmental Chemistry research group, Lyngby, Denmark

The environmental exposure of organisms and humans to chemicals via air, water, soil and food is implemented in the EU tool for the chemical safety assessment (EUSES). The fate of a chemical released to the environment is predicted via a regional level III multimedia model (Simplebox), local models (for water, air and soil systems) and food chain models. These models are based on algorithms and exposure pathways that were developed for neutral and lipophilic chemicals. In many cases they are not valid for polar and ionisable chemicals.

Therefore a multimedia environmental exposure-model applicable for both neutral and ionisable chemicals has been developed from the regional unit environment implemented in Simplebox: the level III-IV Multimedia Activity Model for Ionisable chemicals (MAMI III-IV).

MAMI is based on the chemical activity replacing the traditional approach based on fugacity or

concentration. The chemical activity, or apparent concentration in water, is a convenient model variable as it can be readily defined for neutral and ionic species. The activity approach introduces a new quantity named "activity capacity" to link activities to concentrations.

Chemical equilibrium is defined by equal activities. Diffusion is driven by activity gradients while intermedia advective transport and transformation processes are described by the total concentration. The distribution between neutral and ionic species is described by the Henderson-Hasselbalch equation. Equilibrium between phases is described by species-specific partition coefficients.

The distribution between compartments depends largely on the dissociation status (and therefore the pH) of ionisable compounds, and on the transfer rates of the various species (neutral, ions).

### Quiz solution (from page 10)

Q1: Which structure(s) has(have) most tautomers?

Molecule	#acceptors	#hydrogens	#possibilities	#unique solutions
(A) URIC ACID	7	4	35	24
(B) GUANINE	6	3	20	15
(C) ENPROFYLLINE	5	2	10	8
(D) PURINE-2(3H),6(1H)-DIONE	6	3	20	15

Q2: Which structure(s) has(have) 6 tautomers?

Molecule	#acceptors	#hydrogens	#possibilities	#unique solutions
(W) PIPERAZINE-2,5-DIONE	4	2	4	3
(X) OROTIC ACID	6	3	14	6
(Y) CYTOSINE	4	2	6	6
(Z) BARBITURIC ACID	5	2	5	5

The tautomer structures can be found on the OSIRIS website.

### New OSIRIS Publications

The publication list with [links to the articles](#) is also available at <http://www.osiris-reach.eu>

#### Publications in Peer Reviewed Scientific Journals

- Roncaglioni A, Piclin N, Pintore M, Benfenati E 2008. **Binary classification models for endocrine disrupter effects mediated through the estrogen receptor.** SAR QSAR Environ. Res. 19(7-8): 697-733
- Schüürmann G, Ebert R-U, Chen J, Wang B, Kühne R 2008. **External validation and prediction employing the predictive squared correlation coefficient - test set activity mean vs. training set activity mean.** J. Chem. Inf. Model. 48(11): 2140-2145
- Franco A, Fu W, Trapp S 2009. **Influence of soil pH on the sorption of ionizable chemicals: modeling advances.** Environ. Toxicol. Chem. 28(3): 458-464
- Schwöbel J, Ebert R-U, Kühne R, Schüürmann G 2009. **Modeling the H bond donor strength of -OH, -NH and -CH sites by local molecular parameters.** J. Comput. Chem. 30(9): 1454-1464
- Legind CN, Trapp S 2009. **Modeling the exposure of children and adults via diet to chemicals in the environment with crop-specific models.** Environ. Pollut. 157(3): 778-785
- Jos A, Caméan AM, Pflugmacher S, Segner H 2009. **The anti-oxidant glutathione in the fish cell lines EPC and BF-2: Response to model pro-oxidants as measured by three fluorescent dyes.** Toxicol. in Vitro 23(3): 546-553
- Schwöbel J, Ebert R-U, Kühne R, Schüürmann G 2009. **Prediction of the intrinsic hydrogen bond acceptor strength of organic compounds by local molecular parameters.** J. Chem. Inf. Model. 49(4): 956-962
- Wang B, Chen J, Li X, Wang Y, Chen L, Zhu M, Yu H, Kühne R, Schüürmann G 2009. **Estimation of soil organic carbon normalized sorption coefficient (Koc) using least squares-support vector machine.** QSAR Comb. Sci. 28(5): 561-567
- Böhme A, Thaens D, Paschke A, Schüürmann G 2009. **Kinetic glutathione chemoassay to quantify thiol reactivity of organic electrophiles - Application to  $\alpha,\beta$ -unsaturated ketones, acrylates, and propiolates.** Chem. Res. Toxicol. 22(4): 742-750
- Undeman E, Czub G, McLachlan MS 2009. **Addressing temporal variability when modeling bioaccumulation in plants.** Environ. Sci. Technol. 43(10): 3751-3756
- Fu W, Franco A, Trapp S 2009. **Methods for estimating the bioconcentration factor of ionizable organic chemicals.** Environ. Toxicol. Chem., in press, available online
- Enoch SJ, Cronin MTD, Madden JC, Hewitt M 2009. **Formation of structural categories to allow for read-across for teratogenicity.** QSAR Comb. Sci., in press, available online
- Sihtmäe M, Dubourguier HC, Kahru A 2009. **Toxicological information on chemicals published in the Russian language: contribution to REACH and 3Rs.** Toxicology, in press, available online

### Second OSIRIS Training Course

The next OSIRIS Training Course will be held at the **Mario Negri Institute, Milan, Italy**, on **23-25 September 2009**.

It will comprise both lectures on the concepts underlying the design of Integrated Testing Strategies (ITS) for the regulatory purposes of REACH as well as practical applications of software tools applying ITS .

Details on the programme, venue and registration will be announced on the OSIRIS website <http://www.osiris-reach.eu> .

## Conference Calendar: OSIRIS-related Events

**SETAC Europe 19<sup>th</sup> Annual Meeting**  
31 May – 4 June 2009, Göteborg, Sweden  
<http://goteborg.setac.eu>

**ICCE 2009 - 12<sup>th</sup> EuCheMS International Conference on Chemistry and the Environment**  
European Association for Chemical and Molecular Sciences  
14 – 17 June 2009, Stockholm, Sweden  
<http://www.chemsoc.se/sidor/KK/icce2009.htm>

**PhD course Modeling of plant uptake and application in environmental science and engineering**  
22 – 26 of June 2009, Lyngby, Denmark  
<http://homepage.env.dtu.dk/stt/teaching/start.htm>

**2009 SRA-Europe Annual Meeting**  
Society for Risk Analysis (SRA), Europe regional organisation  
28 June – 1 July 2009, Karlstad, Sweden  
[http://sraeurope.org/index.php?option=com\\_content&task=view&id=47&Itemid=57](http://sraeurope.org/index.php?option=com_content&task=view&id=47&Itemid=57)

**Reduced Animal Testing**  
23 – 24 July 2009, Zurich, Switzerland  
<http://www.mondialresearchgroup.com/index.php?whereTo=ratest>

**10<sup>th</sup> International Conference on Environmental Mutagens (ICEM)**  
International Association of Environmental Mutagen Societies (IAEMS)  
20 – 25 August 2009, Florence, Italy  
<http://www.icem2009.org/>

**VII World Congress on Alternatives & Animal Use in the Life Sciences**  
30 August – 3 September 2009, Rome, Italy  
<http://www.aimgroup.eu/2009/wc7/welcome.html>

**EUROTOX 2009 - 46<sup>th</sup> Congress of the European Societies of Toxicology**  
13 – 17 September 2009, Dresden, Germany  
<http://www.eurotox2009.org/home.asp>

**1<sup>st</sup> Joint PSE-SETAC Conference on Ecotoxicology**  
Ecotoxicology in the real world  
Polish Society of Ecotoxicology, Society of Environmental Toxicology and Chemistry - Central and Eastern Europe Branch  
16 – 19 September 2009, Kraków, Poland  
<http://www.eko.uj.edu.pl/ecotox/2009>

**Environmental Health Risk 2009**  
Fifth International Conference on the Impact of Environmental Factors on Health  
21 – 23 September 2009, New Forest, UK  
<http://www.wessex.ac.uk/09-conferences/environmental-health-risk-2009.html>

**Jahrestagung 2009 der GDCh-Fachgruppe Umweltchemie und Ökotoxikologie**  
German Chemical Society (GDCh)  
23 – 25 September 2009, Trier, Germany  
<http://www.gdch.de/vas/tagungen/tg/5350.htm>

**SETAC GLB Annual Meeting 2009**  
German Language Branch of the Society of Environmental Toxicology and Chemistry  
5 – 7 October 2009, Freising-Weihenstephan, Germany  
<http://www.setac-glb.org/>

**SETAC North America 30<sup>th</sup> Annual Meeting**  
Society of Environmental Toxicology and Chemistry  
19 – 23 November 2009, New Orleans, Louisiana, USA  
<http://www.setac.org/neworleans/>

**EMEC10 - 10<sup>th</sup> European Meeting on Environmental Chemistry**  
1 – 5 December 2009, Limoges, France  
<http://www.unilim.fr/IMG/pdf/Colloque2009.pdf>

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