



# OSIRIS Newsletter

No. 2      December 2008

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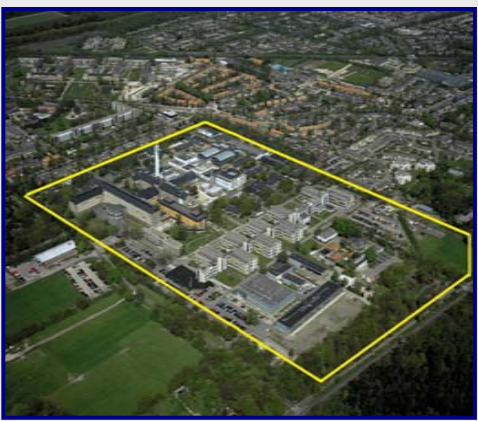


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## Next OSIRIS Annual Meeting



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

RIVM is pleased to host the OSIRIS meeting in the year of its 100 year anniversary. Alternative methods and the 3 R's are important subjects for RIVM.

On the agenda:

- Results of the 2<sup>nd</sup> project year
- Planning for the next months
- Intra- and inter-Pillar/-Workpackage discussions

### OSIRIS Partners



#### Helmholtz Centre for Environmental Research – UFZ (Partner 1)

Department of Ecological Chemistry  
Leipzig, Germany

OSIRIS Co-ordinator, Pillar 1 Co-ordinator, WP 1.2 leader

The Helmholtz Centre for Environmental Research (UFZ) is a governmental research centre belonging to the Helmholtz Association of National Research Centres. It investigates relationships between man and environment under the context of global and climate change.

#### The Department of Ecological Chemistry:

The goal of the Department is to unravel systematic relationships between the molecular structure of compounds and their fate in the environment including biological systems, and to develop methods for predicting their environmental behaviour and toxicity profile. The experimental and theoretical activities focus on two major areas:

- *Environmental Chemodynamics:* Compound partitioning and degradation (photolysis, hydrolysis, biodegradation)



Photo: Norma Neuheiser/UFZ

- *Molecular Toxicology:* Qualitative and quantitative structure-activity relationships (QSARs) including structural alerts to identify substances of concern and provide respective information to support chemical safety assessment and regulatory decision making.

Research is undertaken into computational (*in silico*) methods, chemoassays and non-animal bioassays as components of integrated testing strategies (ITS), and includes method and software development to address QSAR model domain and validation.



#### Liverpool John Moores University – LJMU (Partner 3)

School of Pharmacy and Chemistry  
Liverpool, United Kingdom

Pillar 2 Co-ordinator, WP 2.1 leader

The Liverpool School of Pharmacy at Liverpool John Moores University is the second oldest School of Pharmacy in the United Kingdom (founded in 1849), the University itself now has approximately 20,000 students.

#### Research into QSAR and Modelling:

Research within the area of QSAR and modelling is based within the School of Pharmacy and Chemistry. Researchers working in this area have several decades of expertise in the development of *in silico* models for biological activity, and toxicity in particular.

The researchers investigate the relationships between biological activity and the physico-chemical properties of compounds. This area



Photo: Andrea Richarz

includes the development of Quantitative Structure-Activity Relationships (QSARs) to predict toxicological and pharmacological as well as physico-chemical parameters.

The researchers in QSAR are dedicated to application of these methods to industrial settings and the embedding of the science within the core teaching programs of the School of Pharmacy and Chemistry at Liverpool John Moores University.

### OSIRIS Partners



**National Institute for Public Health and the Environment – RIVM (Partner 5)**

Expertise Centre for Substances  
Bilthoven, The Netherlands

Pillar 3 Co-ordinator, WP 3.2 leader

RIVM is a governmental research and knowledge institute providing policy support to the Dutch Ministry of Health, Welfare and Sport, the Ministry of Environment and Spatial Planning, the Ministry of Agriculture and Fisheries, the National Food Authority, and several National Inspectorates. The national tasks of the RIVM are laid down by law. RIVM is a recognised centre of expertise in the fields of health, infectious diseases, nutrition and food safety, environment and safety.

#### The Expertise Centre for Substances:

The Expertise Centre for Substances (SEC) is the Dutch government expert centre for the risk assessment of chemicals and genetically modified organisms. These tasks are based on national and international regulations and policies regarding these stressors. Examples are



*Photo: RIVM*

Regulation (EC) No 1907/2006 (REACH) and Council Directive 91/414/EEC (Plant Protection Products).

SEC is also actively involved in the development of risk assessment methodology. Pertinent research areas are human and environmental risk assessment, standard setting, (eco) toxicology, (Q)SARs, intelligent testing strategies, emission estimation, probabilistic risk assessment and other methods and models for risk assessment. SEC closely co-operates with other RIVM-units with regard to specialistic expertise needed such as toxicopathology, immunology, environmental chemistry.



**The Netherlands Organisation for Applied Scientific Research – TNO (Partner 7)**

TNO Quality of Life  
Zeist, The Netherlands

Pillar 4 Co-ordinator, WP 4.2 leader

The Netherlands Organisation for Applied Scientific Research (TNO), supports companies and governments with innovative, practicable knowledge. As a statutory organization, TNO has an independent position that allows over 5000 professionals to give objective, scientifically founded judgements.

#### TNO Quality of Life:

The track-record of TNO Quality of Life includes building methods for risk assessment and management, and assessing risks of new and existing substances, pesticides and biocides. TNO participated in experts groups for the revision of the Technical Guidance Documents. Recent European projects include the Strategic Partnership On REACH Testing (SPORT) and the



*Photo: copyright TNO*

REACH Implementation Projects (RIPs) 3.2 and 3.3, including the scoping of the “Exposure Scenarios” and “Intelligent Testing Strategies” concepts.

TNO Quality of Life participates in many European Union projects and has more than fifteen years of experience in the development and application of new methodologies (hazard and exposure) in chemical risk assessment, in close collaboration with industrial partners, regulatory agencies as well as national and international organisations.

### OSIRIS Partners



#### Swiss Federal Institute of Technology Zurich – ETHZ (Partner 10)

Institute for Chemical and Bioengineering  
Safety and Environmental Technology Group  
Zurich, Switzerland

Pillar 5 Co-ordinator, WP 5.1 leader

The Swiss Federal Institute of Technology Zurich is a leading technical university comprising a broad spectrum of basic and applied sciences, including strong departments of environmental sciences and chemistry. The ETHZ is involved in many international collaborations and partnerships, including the Alliance for Global Sustainability with the Massachusetts Institute of Technology, the University of Tokyo, and Chalmers University.

#### The Safety and Environmental Technology Group:

The Safety and Environmental Technology Group at the Institute for Chemical and Bioengineering has been active in the field of chemicals assessment for more than 10 years. The group has contributed to the state of the art in environmental fate and transport modelling.



Photo: Esther Ramseier, © ETH Zürich

Research on chemicals assessment and exposure modelling within the group focuses on models for the global distribution dynamics of persistent organic compounds, models for regional mass balances of organic compounds, methods for inclusion of transformation products in environmental multi-compartment models, metrics of overall persistence and long-range transport potential in the environment, and the methodology of the assessment of persistent, toxic and bioaccumulative (PBT) chemicals.



#### University Rovira i Virgili – URV (Partner 2)

Transport Phenomena Research Team  
Tarragona, Spain

Cross-cutting Co-ordinator of Modelling Work

The Transport Phenomena research team (FeT) includes researchers from the Departments of Chemical Engineering and Computer Science and Mathematics of the University Rovira i Virgili (URV), experts in the areas of chemical and environmental engineering, computer sciences, applied mathematics, artificial intelligence, chemistry, and fluid mechanics-CFD. FeT has the research accreditation of the Catalan Research and Innovation System and is ranked within the top best 5% research groups.

#### FeT Research Focus:

Research interests within OSIRIS include machine learning and data mining, with emphasis on classification and imputation algorithms, dimensionality reduction-feature extraction algorithms and pattern recognition in complex systems of chemical and biological



Photo: <http://www.etseq.urv.es/jet/1.html>

interest, transport of contaminants in the unsaturated soil zone, exposure models, real time predictive identification and control, as well as neurodynamic optimisation.

The team has developed advanced neural network based pattern recognition algorithms and molecular modelling techniques to build robust QSAR / QSPR models for phase transition temperatures (boiling and melting points), critical properties (temperature and pressure), environmental properties such as Henry's Law, solubility or Kow, biological activities, and multimedia fate modelling.

### OSIRIS Partners



#### University of Bern – RIVM (Partner 4)

Centre for Fish and Wildlife Health  
Bern, Switzerland



*Photo: © Universität Bern, Abteilung Kommunikation*

Cross-cutting Co-ordinator of Experimental Work, WP 2.2 leader

The Centre for Fish and Wildlife Health (FIWI) of the University of Bern is internationally recognised for its expertise in the field of fish pathology and fish toxicology. It is the Swiss National Reference Centre for fish diseases, and participates in the network of the European Reference Laboratories. The FIWI has long lasting experience in the development and application of *in vitro* cell systems from fish.

#### FIWI Research Focus:

The toxicological research at the FIWI emphasises the assessment of toxic effects on the basis of mechanistic knowledge and in relation to the cumulative impact of multiple stressors. A key subject in the research of the Centre is to explore the utility of *in vitro*

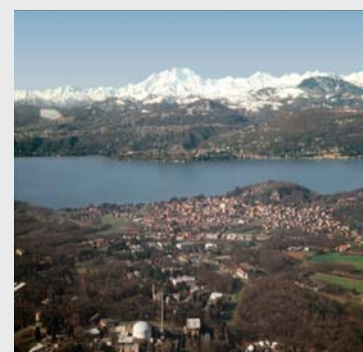
systems for evaluating toxic potencies of chemicals and classifying their modes of action.

Based on this expertise, the FIWI explores within OSIRIS the potential of *in vitro* systems in a tiered testing strategy a) to function as a screening step that, on the one hand, verifies and extends information from non-testing approaches, and, on the other hand, optimises the utilisation of *in vivo* tests, and b) as a tool to replace, reduce or refine *in vivo* testing under REACH.



#### The European Commission's Joint Research Centre – JRC (Partner 26)

Institute for Health and Consumer Protection  
Ispra, Italy



*Photo credit JRC Ispra, printed with permission*

Cross-cutting Co-ordinator of Training Activities (WP 6), WP 4.1, WP 5.3 leader

The mission of the European Commission's Joint Research Centre (JRC) is to provide customer-driven scientific and technical support for the conception, development, implementation and monitoring of European Union (EU) policies. It functions as a reference centre of science and technology for the EU.

The Institute for Health and Consumer Protection (IHCP) is one of the JRC's seven scientific institutes and aims to protect the interests and health of the consumer in the framework of EU legislation on chemicals, food and consumer products. It participates in OSIRIS via the Computational Toxicology Group and the European Centre for the Validation of Alternative Methods (ECVAM).

#### Computational Toxicology Group:

The Computational Toxicology Group promotes the development, assessment, acceptance and

implementation of computer-based methods suitable for the regulatory assessment of chemicals.

This includes methods for predicting the effects of chemicals on human health and the environment, as well as their distribution and fate within the environment and biological organisms.

#### European Centre for the Validation of Alternative Methods:

The role of ECVAM is to support the development, validation and acceptance of methods aimed at reducing, refining or replacing the use of laboratory animals. ECVAM maintains a database on alternative testing methods.

## SETAC Europe Special Science Symposium (SESSS)

### Integrated Testing Strategies for REACH:

#### from Science to Practical Implementation

As first of a new series of conferences organised by SETAC-Europe, the SETAC Europe Special Science Symposium on REACH took place on 23-24 October 2008 in Brussels, Belgium.

The OSIRIS Co-ordinator was member of the Steering Committee and several OSIRIS Partners were speakers. Thus major OSIRIS results were presented to an international audience of stakeholders covering industry, governmental authorities and academia.

#### REACH and Integrated Testing Strategies

The introductory talks (Theo Traas, RIVM; Björn Hansen, Jack de Bruijn, ECHA; Mike Penman, Penman Consulting; Richard D. Phillips, Exxon Mobil) summarised the goals, i.e. to establish an efficient hazard assessment in Europe, allowing on the other hand to reduce animal testing, and requirements of REACH and emphasised the need for international collaboration between industry, regulatory authorities and research institutes. It was stressed that new animal tests should be performed or proposed only as a last resort to fill data gaps. REACH explicitly offers opportunities to use alternative methods and Integrated Testing Strategies (ITS), which have to be further developed for this purpose.

#### Reduction, Refinement: a Critical Appraisal of the Efforts on Reducing Animal Testing

Susanne Bremer, ECVAM, presented activities for validation of alternative *in vitro* methods and stressed the importance of parameters as the biological relevance for the human health endpoint and the applicability domain. John Doe, Syngenta, explained which lessons can be drawn from experience in toxicology for testing under REACH. Thomas Hutchinson, Plymouth Marine Laboratory, reported on environmental ITS approaches, in particular by mode of action.

#### Read Across & QSAR

Mark Cronin, LJMU, demonstrated the applicability of biological read-across: categories formed according to mechanisms of action allow extrapolations of toxicity across species and even across endpoints for reactive chemicals.

Andrew Worth, JRC, reported on qualitative and quantitative structure-activity relationships

(QSARs) and chemical read-across within the context of non-testing strategies for hazard and risk assessment, with examples of useful software and databases.

Gerrit Schüürmann, UFZ, showed the use of structural alerts for screening and evaluation of environmental and human endpoints. They combine chemical reactivity with species sensitivity and enable priority setting for testing. The chemical domain has to be considered carefully.

#### Thresholds of Toxicological Concern

Watzke de Wolf, DuPont, and Helmut Greim, TU Munich, explained the threshold of toxicological concern (TTC) concept, i.e. an exposure value for all chemicals below which no significant risk is expected, and its potential application under REACH for environmental and human toxicology.

Theo Vermeire, RIVM, reported on exposure informed testing under REACH, exposure being one of the decision elements in ITS. He specified the criteria for exposure based waiving (EBW) / triggering (EBT), e.g. based on exposure below a 'no further action level' or exposure scenarios.

#### Risk Assessment & Decision Making

Frédéric Bois, INERIS, presented probabilistic approaches to estimate uncertainties and guide decisions about testing strategies.

Dinant Kroese, TNO, reported on a weight of evidence (WoE) approach being developed for ITS based on a computerised decision theory framework. It incorporates existing data, grouping and read-across, QSARs, TTC, exposure and *in vitro* information, is flexible for adaptations and includes cost-effectiveness analysis.

José Tarazona, INIA, explained the quantitative and qualitative risk characterisation foreseen for dangerous substances under REACH.

Ortwin Renn, Univ. Stuttgart, showed that risk communication including the communication of uncertainties is a necessary part of risk management, linking risk analysis and perception.

The Symposium included also break-out sessions on case studies, poster exhibitions and demonstrations of tools and services to support REACH testing and registration.

## Second OSIRIS Stakeholder Workshop

The Second OSIRIS Stakeholder Workshop took place on 17 November 2008 in Brussels, Belgium, organised by the OSIRIS Partner DIALOGIK.

### Introduction to Risk Assessment and ITS

The OSIRIS Co-ordinator Gerrit Schüürmann, UFZ, explained that the rationale behind applying Integrated Testing Strategies (ITS) is the 3R concept, i.e. the replacement, reduction and refinement of animal testing. Using ITS, however, there is no one-by-one replacement, but several different approaches are combined and considered instead.

Georges Deschamps, DG Science and Research, European Commission, stressed the importance and the global dimension of the chemicals risk assessment.

Evelin Fabjan, European Chemicals Agency, summarised the information requirements under REACH and showed that REACH gives a framework for application of ITS and the opportunity to use alternative methods.

### Presentation and Discussion of Current OSIRIS Project Results

Mark Cronin, LJMU, summarised the results from Pillar 2 (Biological Domain) regarding the major topics, e.g. the collection and structuring of toxicological databases, evaluation of data quality, the application of mode and mechanism of action information in ITS, formation of categories for read-across and the optimisation of proposals for *in vivo* testing.

Theo Vermeire, RIVM, explained the concept of exposure based waiving (EBW) and triggering (EBT) and their applications and limitations within REACH. EBW should be justified by a thorough exposure assessment. Pillar 3 (Exposure) is concerned with the improvement of EBW models, uncertainty analysis and integration of EBW/EBT into ITS.

Bette Meek, University of Ottawa, emphasised the importance of priority setting of chemicals as well as of analysing earlier facts and establishing the applicability domain.



Dinant Kroese, TNO, showed the need for a formal weight of evidence (WoE) framework to integrate the different types of information. It should allow for transparency, quantify the uncertainties and resolve conflicting values. He presented the concept of the OSIRIS web tool implementing the ITS developed and conceived to help the user to comply with REACH. It uses only publicly available databases and accepts testing data from the end-user.

Watzke de Wolf, ECETOC, stressed the elements for success of the OSIRIS ITS tools: matching the REACH information needs, delivery on time, acceptance by all parties involved, accessibility and sustainability.

### Group Discussions of 3 Major Issues

- Under which conditions are the proposed ITS operational for use under REACH?
- Is the existing information sufficient to use ITS or which additional information is needed?
- Is it possible to reduce testing, especially animal testing, without limitations in accuracy, validity and reliability?

For this discussion the Carousel method was used: Each question was discussed in a small group of 5 persons, questions and groups were switched twice after 20 minutes, respectively.

The feedback received will be taken into account for further planning of the OSIRIS project.

A more detailed report of the Workshop is being prepared by DIALOGIK and will be made available through the OSIRIS website <http://www.osiris-reach.eu>.

### OSIRIS Publications

#### Publications in Peer Reviewed Scientific Journals

- Trapp S, Cammarano A, Capri E, Reichenberg F, Mayer P 2007. **Diffusion of PAH in potato and carrot slices and application for a potato model.** Environmental Science and Technology 41: 3103-3108
- Mortimer M, Kasemets K, Heinlaan M, Kurvet I, Kahru A 2008. **High-Throughput Kinetic Vibrio fischeri bioluminescence inhibition assay for study of toxic effects of nanoparticles.** Toxicology in Vitro 22: 1412-1417
- Trapp S, Ma B, Bomholtz L, Legind CN 2008. **Coupled mother-child model for bioaccumulation of POPs in nursing infants.** Environmental Pollution 156: 90-98
- Benigni R, Bossa C, Richard AM, Yang C 2008. **A novel approach: chemical relational databases, and the role of the ISSCAN database on assessing chemical carcinogenicity.** Ann. Ist. Sup. San. 44: 48-56
- Franco A, Trapp S 2008. **Estimation of the Soil-Water Partition Coefficient Normalized to Organic Carbon for Ionizable Organic Chemicals.** Environ. Toxicol. Chem. 27(10): 1995-2004
- Porcelli C, Roncaglioni A, Chana A, Benfenati E 2008. **A comparison of DEMETRA individual QSARs with an index for evaluation of uncertainty.** Chemosphere 71: 1845-1852
- Navas JM, Segner H 2008. **In-vitro screening of the antiestrogenic activity of chemicals.** Expert Opinion in Drug Metabolism and Toxicity 4(5): 1-13
- Trapp S, Rosania GR, Horobin RW, Kornhuber J 2008. **Quantitative modeling of selective lysosomal targeting for drug design.** European Biophysics Journal 37: 1317-1328
- Enoch SJ, Hewitt, M, Cronin MTD, Azam S, Madden JC 2008. **Classification of chemicals according to mechanism of aquatic toxicity: An evaluation of the implementation of the Verhaar scheme in Toxtree.** Chemosphere 73: 243-248
- Mayer P, Holmstrup M 2008. **Passive Dosing of Soil Invertebrates with Polycyclic Aromatic Hydrocarbons: Limited Chemical Activity Explains Toxicity Cutoff.** Environmental Science and Technology 42: 7516-7521
- Kahru A, Dubourguier HC, Blinova I, Ivask A, Kasemets K 2008. **Biotests and Biosensors for Ecotoxicology of Metal Oxide Nanoparticles: A Minireview.** Sensors 8: 5153-5170
- Bönnhardt A, Kühne R, Ebert R-U, Schüürmann G 2008. **Indirect photolysis of organic compounds: prediction of OH reaction rate constants through molecular orbital calculations.** J. Phys. Chem. A. 112(45): 11391-11399
- Franco A, Fu W, Trapp S 2008. **The influence of soil pH on the sorption of ionizable chemicals: modelling advances.** Environ. Toxicol. Chem., in press, preprint available online
- 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., in press, available online
- Schwöbel J, Ebert R-U, Kühne R, Schüürmann G 2008. **Modelling the H Bond Donor Strength of -OH, -NH and -CH Sites by Local Molecular Parameters.** J. Comput. Chem., in press, available online

#### Scientific Reports

- Netzeva T, Pavan M, Worth AP 2007. **Review of Data Sources, QSARs and Integrated Testing Strategies for Aquatic Toxicity.** EUR 22943 EN. Joint Research Centre, Institute for Health and Consumer Protection, Ispra, Italy
- Patlewicz G, Worth A 2008. **Review of Data Sources, QSARs and Integrated Testing Strategies for Skin Sensitisation.** EUR 23225 EN. Joint Research Centre, Institute for Health and Consumer Protection, Ispra, Italy
- Vermeire TG et al. 2008. **Exposure informed testing under REACH.** Report 601017001. RIVM, Bilthoven; TNO, Zeist, The Netherlands



## OSIRIS Results Highlights

### Review of Existing Models, Data Sources and Strategies (Partner JRC)

At the start of the OSIRIS project, existing models, e.g. expert systems and quantitative structure-activity relationship (QSAR) models, sources of toxicity data and current thinking of integrated testing strategies (ITS) have been reviewed for one environmental and one human endpoint, i.e. aquatic toxicity and skin sensitisation, in order to guide further work.

The emphasis of the reviews was on the usefulness of the models for regulatory assessment of chemicals, particularly for the purposes of REACH.

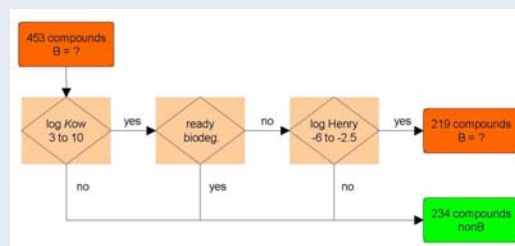
In addition to traditional data sources such as databases, papers publishing experimental data have been identified. General (global) models as well as models for specific chemical classes and mechanisms of action have been summarised. Regarding aquatic toxicity, effects on organisms from three trophic levels (fish, Daphnia and algae) have been considered.

These reviews are publicly available as JRC reports EUR 22943 EN and EUR 23225 EN. They can be downloaded from <http://ecb.jrc.ec.europa.eu/qsar/publications/>.

### Screening Criteria for Substance-specific Waiving of Bioassays (Partner AL)

Physicochemical properties, e.g. solubility, volatility, distribution and persistence condition the behaviour of chemicals regarding media-specific exposures and bioavailability in test systems. The differential influence of these properties have been analysed to identify criteria for substance-specific waiving of experimental bioconcentration studies.

Exploratory data analyses revealed effective cut-off criteria in lipophilicity ( $\log K_{ow}$ ), Henry constant (presumably combining information about water solubility and volatility) and ready biodegradability. These three parameters were combined in a preliminary decision tree.



Preliminary decision tree to support identification of nonB compounds as candidates for waiving of experimental BCF studies.

The system has been optimised to be protective, i.e. there are no false negatives (sensitivity of 100 %), in order to reliably identify nonB compounds (bioconcentration factor BCF < 2000). The result indicates a reduction potential of animal test candidates for bioaccumulation by 50 %.

### Prototype of the Intelligent Testing Framework Web Tool (Partners SIMPPLE, TNO, RIVM)

The Integrated Testing Strategies (ITS) fit for REACH developed in the OSIRIS project are being implemented in a web tool, with the objective to support the use of non-testing information for regulatory decision making.

A first prototype has been made available to the project partners to offer an operative platform for validation and quantitatively testing of the initial and subsequent decision-based ITS.

Two endpoints are addressed in this first version: bioconcentration factor and mutagenicity.

The tool is conceived to be able in future versions to integrate results from several non-

testing methods using a weight-of-evidence (WoE) approach, handle uncertainty and make decisions based on all available information.



The user can manage substances, test data, *in silico* data and physico-chemical properties of the substances. He can also create assessments and apply them to evaluate substances using the implemented ITS. The tool also allows the user to manage the expert judgements required.

## OSIRIS Results Highlights

### Exposure informed testing under REACH (Partners RIVM, TNO)

Exposure is one of the decision elements in integrated testing strategies (ITS). Testing can be waived (EBW = Exposure-Based Waiving) or triggered (EBT = Exposure-Based Triggering) on the basis of exposure considerations.

An inventory of waiving options under REACH for human and environmental endpoints has been made including a discussion of the qualitative and quantitative justifications needed for EBW/EBT.

Qualitative argumentation can be applied when certain exposure pathways are obviously irrelevant, e.g. due to physico-chemical substance properties. Quantitative justifications depend on the availability of effect levels of no concern

such as PNECs (predicted no-effect concentrations), DNELs (derived no-effect levels) and TTCs (thresholds of toxicological concern).

Examples of EBW/EBT situations and criteria have been provided for direct, external exposure of consumers and workers, environmental exposure and internal (systemic) human exposure.

Planned further work includes 1) the development of criteria for models to be suitable for the exposure assessment required for EBW and the analysis of the models available; 2) the analysis of exposure model uncertainty.

This review is publicly available as RIVM report 601017001 at <http://www.rivm.nl/bibliotheek/rapporten/601017001.html>.

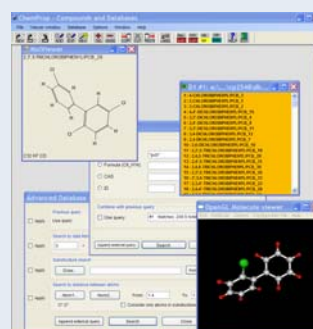
### Database with Substructure/Data Search and Structure Import/Export (Partner UFZ)

Within the OSIRIS project, a large number of compound-related data sets will be built. The data sets cover physicochemical, toxicological and ecotoxicological data within the chemical domain of REACH for risk-targeted prioritisation. To organise all these data in a suitable manner, a central OSIRIS database is required.

This database system developed enables substructure and data searching, as well as structure import/export through SMILES and other standard formats for chemical structures.

It is designed to contain information on the chemical structures together with identifying

information and some basic compound properties. Other data will be contained in external, specialised databases, which can be maintained separately. The link to them is provided by the central database. The key to share any information between the separate databases is a compound identification number registered in the central database. The approach also supports confidential data.



### Decision model for cost-effectiveness analyses (Partner WUR)

A general framework for cost-effectiveness analysis (CEA) for toxicological tests of chemicals has been suggested. The framework applies to any type of chemical test, including ITS. The aim is to allow for comparing various types of tests in order to gain information on test performance based on costs and effects, including animal welfare.

In the context of REACH, three types of decision-makers can be distinguished, i.e. the social planner or regulator, the private decision maker (chemical producers and manufacturers), and the test developer. For each decision-maker the decision-problem has been characterised.

Applying CEA to different types of decision-problems provides a ranking of tests according to their incremental cost-effectiveness ratio (ICER), which denotes (average) additional costs per additional (average) unit of effect. By means of additional information on a decision-maker's budget of the willingness-to pay for an additional unit of effect CEA serves as decision-support tool for choosing those tests (or testing strategies) that perform best given available resources.

This provides guidance for optimally allocating scarce resources on different types of tests and testing strategies.

### Conference Calendar: OSIRIS-related Events

#### **EMEC9 - 9th European Meeting on Environmental Chemistry**

Association of Chemistry and the Environment  
3-6 December 2008, Girona, Catalonia, Spain  
<http://www.udg.edu/tabid/10391/Default.aspx/Welcome/tabid/10391/language/ca-ES/Default.aspx>

#### **Lhasa Symposium: New Horizons in Toxicity Prediction**

Symposium in collaboration with the University of Cambridge  
8-9 December 2008, Cambridge, UK  
<http://www.lhasasymposium.com/>

#### **SETAC Europe 19th 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>

#### **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>

#### **14th International Workshop on Quantitative Structure-Activity Relationships (QSARs) in Environmental Sciences**

24-28 May 2010, Montreal, Canada  
<http://www.qsar2010-montreal.com/>

#### **IUTOX-2010 - XII International Congress of Toxicology**

Spanish Association of Toxicology (AETOX) EUROTOX in the name of the International Union of Toxicology (IUTOX)  
11-15 July 2010, Barcelona, Spain  
<http://gestion.pacifico-meetings.com/www/iutox2010/>

### Next OSIRIS Training Course

The next OSIRIS Training Course is scheduled for September 2009.

It will focus on the practical application of integrated testing strategies (ITS) and corresponding software tools.

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

Responsible for the  **Newsletter** : Dr. Andrea Richarz  
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OSIRIS is a EU 6th Framework Integrated Project,  
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