OSIRIS Newsletter

No. 7 July 2010

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Third OSIRIS Training Course

3—5 November 2010 • Milan, Italy

The Third OSIRIS Training Course will be held on **3-5 November 2010** at the **Mario Negri Institute** in **Milan, Italy**.

It will comprise both lectures on basic concepts underlying chemical safety assessment and the REACH regulatory framework as well as practical software and web tool demonstrations.

The training will cover several topics related to **risk assessment** and **Integrated Testing Strategies** (ITS) fit for REACH.

A special section of the course will be devoted to the **practical application of QSAR** (qualitative or quantitative structure-activity relationship) **and expert system tools** for predicting a human endpoint (mutagenicity / genotoxicity) and an environmental endpoint (bioconcentration factor). A number of case studies will be presented.

Details on the programme, venue and registration will be announced on the OSIRIS website **www.osiris-reach.eu** .

Photo: Andrea Richarz

Presentation of OSIRIS in ECHA

An OSIRIS delegation consisting of Gerrit Schüürmann, UFZ (Co-ordinator), Dinant Kroese, TNO and Theo Vermeire, RIVM met with representatives from the European Chemicals Agency (ECHA) on 27 May 2010 with the aim to:

- give a general overview of the project, its aims, structure, participants and current achievements,
- get a common understanding on basic principles of integrated testing strategies (ITS), provide examples and illustrate their possible application for regulatory purposes,
- present the ways OSIRIS handles chemical exposure, possibilities for exposure based waiving (EBW) and tools available to support that process.

Overview of the EU Integrated Project

The goal of OSIRIS is to develop ITS enabling to significantly increase the use of non-testing information for regulatory decision making, and thus to minimise the need for animal testing in the context of REACH. The ITS include alternative methods such as chemical and biological read-across, chemical category formation, qualitative and quantitative structure-activity relationships (QSARs), chemoassay screening, *in vitro* information, thresholds of toxicological concern (TTC), and exposure based waiving. Methods to address uncertainty, cost-benefit analyses, Weight-of-Evidence reasoning and consensus modelling are taken into account.

OSIRIS Weight-of-Evidence Approaches

In order to successfully replace *in vivo* testing (or at least reduce or refine it) an objective methodology should assess whether the alternative data suffice for its purpose, i.e. provide sufficient and adequate information to allow conclusions on classification and labelling for the endpoint considered, and for deriving DNELs (DMELs). Weight-of-Evidence methodologies are being developed for both categorical and continuous endpoints, focussing on ITS

Photos: Copyright European Chemicals Agency

for the human health endpoints skin sensitisation, mutagenicity, carcinogenicity, and repeated dose toxicity (also as surrogate for reproductive toxicity) as well as for the environmental endpoints bioconcentration and aquatic toxicity. The ITS are being implemented in a webbased tool which will be made publicly available.

OSIRIS and Exposure Based Waiving

Exposure based waiving is a potentially important element in testing strategies to reduce animal testing and therefore one of the OSIRIS Pillars.

The principle behind any EBW is that there are situations when human or environmental exposures are so low or infrequent that there is a very low probability that the acquisition of additional effect information may lead to an improvement in the ability to manage risk. EBW therefore is risk based and needs thorough knowledge on exposure as well as on no-effect criteria.

REACH only allows EBW in a limited number of cases with constraints on tonnage levels, types of tests to be waived and the need for a thorough exposure scenario and exposure assessment throughout the life cycle of a chemical and for all human exposure routes and environmental pathways.

Discussions with ECHA representatives

Scientific and technical aspects of the presented methods and approaches were discussed. The *in silico* tools developed within OSIRIS raised interest as well as the new database on mammalian toxicity derived from Russian-language sources. ECHA is interested in testing the gamma-version of the OSIRIS web tool in autumn 2010.

Ways towards further involvement of ECHA in OSIRIS were discussed as well as the question how to organise maintenance of OSIRIS software tools beyond project lifetime.

Data Quality Assessment for *in silico* Methods: A Survey of Approaches and Needs

A **joint action of 21 contributors from 12 OSIRIS partner institutions** (AL, RIVM, IRFMN, ISS, LJMU, FhG, URV, WUR, IVZRS, TNO, UB, MERCK) has presented common grounds for data quality within (and beyond) OSIRIS from **different (inter)disciplinary perspectives**. The project report will be published as a chapter of the book "*In Silico Toxicology. Principles and Applications*" edited by M. Cronin and J. Madden (LJMU).

Integrated Testing Strategies (ITS) aim to use and combine existing data for human and environmental risk assessment purposes while minimising the need for new testing. REACH has advocated a Weight of Evidence (WoE) approach to decide whether information is adequate to draw a conclusion on, e.g., the toxicological properties of a substance. To determine how much a piece of information should contribute to the overall conclusion, the validity of methods needs to be assessed as well as the reliability and relevance (fit-for-purpose) of this information.

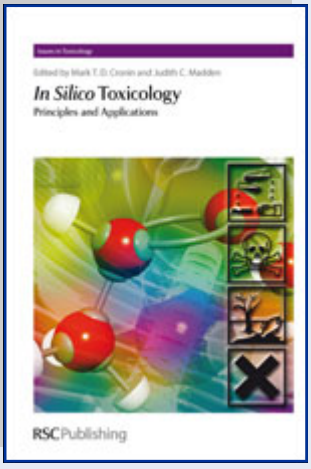
Data quality assessment needs to address multiple issues at several levels:

- **Individual data quality:** The variability in pieces of information depends on confounding factors in the (experimental) procedure used to generate the data. *In silico* predictions must include an assessment, at the very least, of the error range of the experimental data that were used to derive the model. Variability of toxic effect data can be due to either technical (e.g., identity of test substance, deviations of test protocols, differences in exposure conditions) or inherent biological (e.g., species, strain, age and sex of test animals, seasonal influence) factors.
- **Combined data quality:** Less reliable data can still be adequate for risk assessment in combination with other evidence. The pooling of several studies, one or more of which may be inadequate by itself, may collectively satisfy the overall requirement for valid data.
- **Context-dependent data quality:** Different levels of data quality are required for different purposes. For example, read-across requires a very high confidence in each of the few data points it uses; Qualitative/quantitative structure-activity relationships (QSARs) demand increasing confidence in the experimental input data with decreasing number of substances in the training/test set; and evidence-based toxicology (EbT) may cope with mixed variability.

Variability is an obvious first measure of data quality, but what is actually required is an **understanding of the degree of (un)certainty**. The ultimate objective of data quality assessment is to identify, reduce and communicate uncertainty in decisions based on data. The acceptable uncertainty of data (measured or generated *in silico*) in the regulatory context depends on the outcome of the hazard identification and risk assessment and can also be weighted for the "cost" of errors.

Data quality assessment is a complex and time-consuming task, but exceptionally important as models derived from poor quality data will only deliver poor predictions. The OSIRIS report supports and encourages the crucial process of data quality assessment with a focus on specific needs in *in silico* toxicology by providing

- common terms and definitions,
- background information on formal data quality scoring schemes,
- description of chemical and biological factors of data variability,
- checklist approaches to data quality assessment,
- data quality considerations for physico-chemical data, calculated QSAR descriptors as well as environmental and human toxicity,
- data quality needs in data integration and socio-economic evaluations of ITS by means of cost-effectiveness analysis.



Nendza M, Aldenberg T, Benfenati E, Benigni R, Cronin M, Escher S, Fernandez A, Gabbert S, Giralt F, Hewitt M, Hrovat M, Jeram S, Kroese D, Madden J, Mangelsdorf I, Rallo R, Roncaglioni A, Rorije E, Segner H, Simon-Hettich B, Vermeire T 2010. Data quality assessment for *in silico* methods: A survey of approaches and needs.

In: Cronin M, Madden J (eds): *In Silico* Toxicology. Principles and Applications, RSC Publishing, Cambridge, UK

Forthcoming in autumn 2010.

OSIRIS Results Highlights

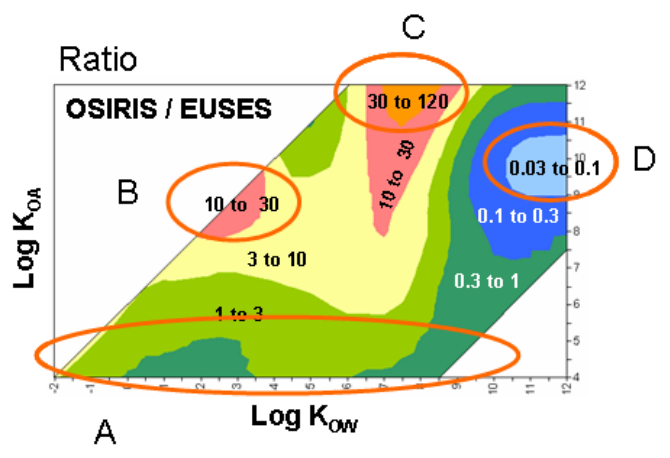
Comparison of new OSIRIS models to the EU regional model for environmental exposure (EUSES) (Partners SU, DTU, ETHZ)

Stockholm University, Department of Applied Environmental Science, Sweden; DTU Ecotoxicology and Environmental Chemistry Research Group, Lyngby, Denmark; ETH Zurich, Safety and Environmental Technology Group, Switzerland

Comparison of models for bioaccumulation

An spLFER (single parameter linear free energy relationship) version of the OSIRIS model for bioaccumulation (SU) was compared to the EUSES model (also based on spLFERs). The models predict the total daily dose of a chemical to a human based on the chemical's concentrations in air, water, soil, and sediment. Total daily doses were estimated for hypothetical persistent chemicals (i.e. no biotransformation) assuming equilibrium partitioning between air, water, soil and sediment.

The model comparison identified regions of the chemical partitioning space where i) the two models generated similar results (A) ii) the OSIRIS model generated substantially higher daily doses (B, C) and iii) the OSIRIS model generated substantially lower daily doses (D) (see figure). The comparison shows that the **OSIRIS model** in general **predicts significantly higher human daily doses** for all but the super hydrophobic chemicals. The difference between the models was particularly striking for high K_{OW} and high K_{OA} compounds due to significantly higher concentrations in fish predicted by OSIRIS, and the very high concentrations in root crops predicted by EUSES. The regression employed in EUSES to calculate uptake of chemicals from soil yielded a comparatively low uptake of hydrophilic compounds in vegetation, which in turn resulted in lower intake via this exposure vector than in the OSIRIS model.



Ratio between the daily dose (kg chemical kg^{-1} body weight) estimated by OSIRIS and EUSES (DoseOSIRIS/DoseEUSES), plotted as a function of the log octanol-air (K_{OA}) and log octanol-water (K_{OW}) partition coefficients, assuming emissions to air only and no biotransformation.

Comparison of new multispecies models to the single-species EUSES model

The Multimedia Activity Model for Ionics (MAMI, DTU) is designed to predict the environmental fate of neutral and ionisable chemicals, the Multi-Species Multi-Media model (MS-MM, ETHZ) includes the fate of degradation products that result from the breakdown of an emitted chemical in the environment. A single-species model identical to the regional scale of Simplebox (the exposure model implemented in EUSES) was developed as reference.

The comparison of MAMI with EUSES highlighted the **impact of dissociation and pH on the partitioning constants of ionisable substances**. The species specific estimations for the K_{OC} in MAMI differ remarkably from the regressions implemented in the EUSES regional model. The latter neglect the impact of pH and electrical interactions on the sorption to solids and likely underestimate PECs of organic bases in soil and sediments.

For the MS-MM model, the most important impacts were on **determination of chemical persistence** — including degradation products would increase the number of substances classified as persistent and very persistent under REACH —, the choice of whether testing should consider **single-chemical or multi-component (mixture) toxicity**, and whether degradation products could **trigger tests**, such as sediment or soil toxicity tests that would not be triggered by the parent compound alone.

The degradation pathway of organic chemicals often includes ionisable metabolites. The **combined use** of the MS-MM model for **degradation products** and the activity model for **neutral and ionics** MAMI provides a robust model framework for high tier exposure assessment of multispecies chemicals.

OSIRIS Results Highlights

Such a combined use may indeed be necessary given that the fate of ionisable metabolites that are persistent and accumulate in soil and sediment compartments may dominate aspects of chemical classification (based, e.g., on persistence) and on the waiving or triggering of specific tests (e.g. whether a sediment toxicity test is warranted).

A challenge for risk assessment: ionisable compounds in the REACH chemical space (Partner DTU)

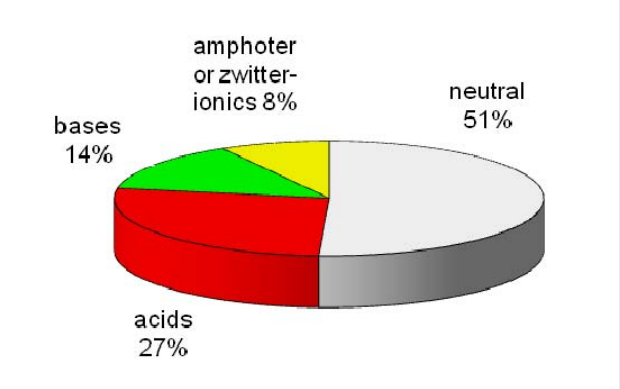
DTU Ecotoxicology and Environmental Chemistry Research Group, Lyngby, Denmark

The diversity of compounds classes within the REACH chemical space represents a major challenge for risk assessors. **Ionisable organic groups** such as carboxylic acids, phenols, amines and anilines, are frequent **in many organic industrial chemicals**. A particular class of ionisable organics are ionic surfactants, very frequent in detergents, dyes, pigments, adhesives and other products. To better characterise the poorly known occurrence of ionisable organics among industrial chemicals, a screening study was performed on a representative sample of substances pre-registered to the EU Regulation for the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

About 143 000 industrial chemicals have been pre-registered at the European Chemicals Agency to comply with REACH (ECHA 2009a). A representative random sample (1.5% out of the approximately 117 000 substances due to registration in 2010 and 2013) was selected and processed using the software ACD/Labs® to calculate the dissociation constant(s) (p*Ka*), the octanol-water partition coefficient of the neutral molecule (log K_{OW}) and the vapour pressure of the neutral molecule (p_s).

Almost **one half** of the screened compounds are **at least partially ionised** under environmentally relevant conditions (pH 4 to 10) (see figure). Among these, most are acids (27%), but also bases (14%), amphoters and zwitterionics (8%, molecules including both acidic and basic groups) are common.

Most substances have log K_{OW} ranging between 0 and 4. **Hydrophilic chemicals** are **most frequent** (30% with log K_{OW} < 1) but super-hydrophobic chemicals are present as well (10% with log K_{OW} > 6). About 28% of these very **super-hydrophobic**, i.e. 3% of the total sample analysed, are mostly ionised at pH 7. Long lipophilic structures with an ionisable head (e.g. surfactants) fall into this category.



Percentage of ionics from 1510 pre-registered REACH chemicals. Only acid p*Ka* < 12 and basic p*Ka* > 2 are considered.

REACH chemicals generally exert **low vapour pressure**: p_s < 1 Pa for 65% and > 100 Pa for only 13%. The apparent volatility may be even lower due to ionisation, because the vapour pressure of ionic species is negligible.

Two **major challenges** were identified with regard to **risk assessment** of ionisable chemicals. First, estimations models are often not applicable to ionisable chemicals. Secondly, additional test requirements may be needed to cover both sides of the environmentally relevant pH-range (ECHA 2009b). The results of this screening study highlight the need to **extend the applicability domain** of existing models and **refine model predictions**, taking into account the effect of pH.

References

ECHA European Chemical Agency 2009a. REACH Guidance Documents. http://guidance.echa.europa.eu/guidance_en.htm

ECHA European Chemical Agency 2009b. ECHA publishes an updated list of pre-registered substances. Press release ECHA/PR/09/03. http://echa.europa.eu/doc/press/pr_09_03_list_prereg_substances_20090327.pdf

Additional information: Franco A, Ferranti A, Davidsen C, Trapp S 2010. An unexpected challenge: ionizable compounds in the REACH chemical space. Int. J. LCA 15: 321–332

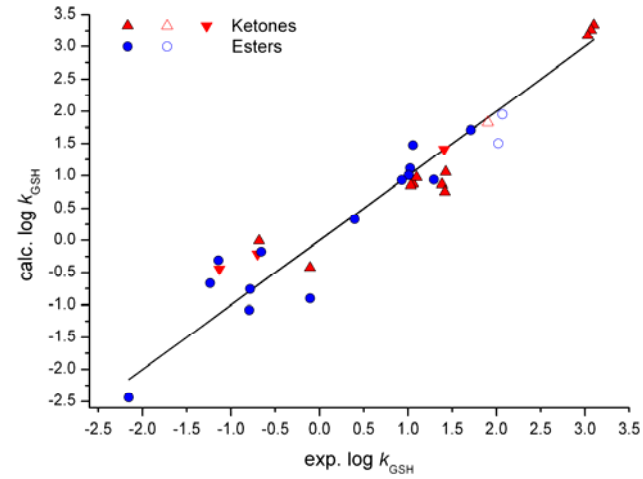
OSIRIS Results Highlights

Prediction of the toxicity-relevant reactivity by local electrophilicity (Partner UFZ)

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

Electrophilic substances are able to form covalent bonds to **nucleophilic reaction sites** in proteins and DNA. This results in **reactive toxicity** and associated diseases such as dermal or respiratory sensitisation and mutagenicity. For this reason, the prediction of the reactive behaviour of electrophilic compounds as potential reactive toxicants is of great importance for the risk assessment of chemicals., e.g. in the context of the EU regulation for industrial chemicals REACH. ***In silico* approaches** as alternative methods for hazard and risk assessment could facilitate the evaluation of chemical substances.

In view of a quantitative **prediction of electrophilicity** based on the molecular structure, two new **local electrophilicity parameters** $\omega^{q}_{r,s}$ and $\omega^{E}_{r,s}$ were derived, using site-specific quantum chemical parameters for the quantification of the energy change associated with the gain or loss of electronic charge, since these reactions are driven by the electron transfer from the nucleophile to the electrophile.



Log k_{GSH} of 31 *a,β*-unsaturated carbonyl compounds calculated using $\omega^{q}_{=O,\beta C}$ versus the experimental values. Circular symbols represent esters, triangular symbols ketones, with cyclic compounds indicated through downward triangles. Filled symbols refer to Michael systems with a C=C double bond, open symbols to C≡C−C=O systems. The solid line indicates identity.

Both local electrophilicity parameters showed superior behaviour within two test cases compared to previous approaches such as Parr's global electrophilicity ω or its local variant ω_r^+ using condensed-to-atom Fukui functions.

In the first test case both parameters were used to **predict experimental reaction rate constants** of a set of 31 *a,β*-unsaturated carbonyl compounds towards the **model nucleophile glutathione**, an antioxidant protecting cells from reactive electrophilic species. As glutathione is highly available within the cytoplasm, it is supposed to react with most electrophiles in the first place, thereby protecting proteins and DNA up to the point at which its concentration is critically decreased. We were able to reproduce the logarithmic experimental reaction rate constants of the test set consisting of 15 ketones and 16 esters via multi linear least squares regression yielding r^2 (squared correlation coefficient) values up to 0.95.

The second data set demonstrates the suitability of the new reactivity parameters to **model Mayr's electrophilicity parameter *E*** for 20 benzhydrylium cations by yielding r^2 values up to 0.99. The parameter *E* forms the basis of an experimentally derived electrophilicity scale and is used in combination with two nucleophile dependent parameters to compute reaction rate constants for electrophile−nucleophile reactions. The experimental determination of these three parameters is difficult, hence they are available only for the minority of toxicologically relevant substances. In this context, the prediction of the parameter *E* is a promising first step towards the extension of Mayr's electrophilicity scale without further need of experimental work.

Both results indicate the suitability of the two new local electrophilicity parameters to **screen organic compounds *in silico*** for their electrophilic reactivity in general, and for their potential to exert reactive toxicity in particular.

Additional information: Wondrousch D, Böhme A, Thaens D, Ost N, Schüürmann G 2010. Local electrophilicity predicts toxicity-relevant reactivity of Michael acceptors. J. Phys. Chem. Lett. 1: 1605–1610

OSIRIS Results Highlights

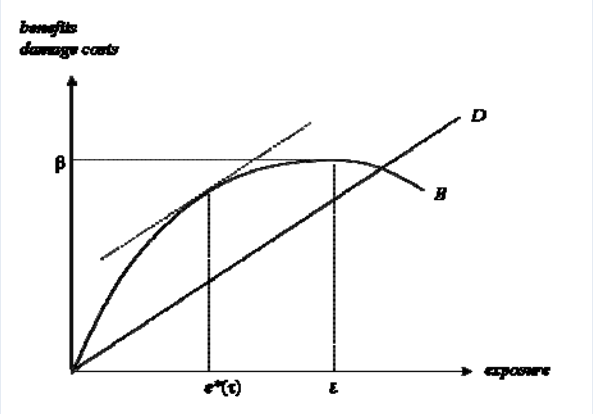
A decision analytic value-of-information approach for test evaluation (Partner WUR)

Wageningen University, Environmental Economics and Natural Resources Group, The Netherlands

Risk management of chemicals requires information about their adverse effects such as, for example, toxicity and persistence. Testing of chemicals allows for improving the information base for regulatory decision-making on chemicals' production and use. Testing a large number of chemicals with limited time and resources forces a prioritisation of testing, i.e. a rank order of chemicals such that higher ranked substances are to be tested earlier than lower ranked substances. A **decision model for the prioritisation of chemicals** for testing has been developed: The model adopts a value-of-information (VOI) approach describing the expected welfare gains from regulatory actions that respond to test information revealing chemicals' level of toxicity and persistence. Hence, the VOI model suggested can be applied to both human health and environmental endpoints. The **expected welfare gain** of improved regulation is the **value of information**.

It is assumed that exposure (e), is the variable that the regulator can control. Hence, safety measures are modelled as a **reduction of exposure** to toxic or potentially toxic chemicals. As shown in the figure, in the absence of regulations the maximum benefits that could be obtained from the use of a substance are β (i.e. where marginal benefits equal zero). Thus, ε denotes the unregulated level of exposure when damages are externalities and are not accounted for.

Given safety measures e, the substance should **only** be **produced if benefits** (B) **exceed the damage** (D) from the use of a substance, i.e. if $B(e) \geq D(e,\tau)$ with τ denoting a substance's toxicity potential. The optimal regulation, i.e. the optimal expected level of exposure $e^*\tau$, is where marginal benefits equal marginal damage, which is given by the solution to $\max_e [V = B(e) - e\,E(\tau)]$ (with E denoting the expectations operator). The expected VOI is the expected gain when using the substance if optimally regulated with additional information from testing, instead of using the substance regulated under uncertainty. A test should be performed if and only if its VOI exceeds its costs.



If the VOI from testing net of costs of testing differs between two substances, then the **test with the higher net value of information** should be **performed first**. In this way all substances can be prioritised with regard to testing. Hence, ultimately, the VOI is driven by the **effectiveness of regulatory actions** which determine human and environmental exposure to chemicals.

The analysis generally **supports** the use of the **prioritisation criteria adopted in REACH**. Chemicals known as highly toxic or highly persistent should be tested first because the required testing offers a higher VOI than testing substances without evidence of either toxicity or persistence. This effect is particularly strong if persistence is known, which supports the early deadline for substances already classified as PBT or vPvB as adopted in REACH. In addition, the decision-model accounts for **other relevant prioritisation criteria** that REACH ignores. For example, test prioritisation depends on the VOI *net of testing costs*. **Testing costs** may differ substantially between substances, for example when prior information differs. Hence, a regulator who sets the rules for prioritisation cannot disregard testing costs but must balance the welfare gains from improved regulation against the costs. This holds in particular if testing costs do not only comprise direct monetary costs but also include animal welfare loss. Accounting for testing costs may trigger the development of more efficient testing strategies such as, for example, Integrated Testing Strategies (ITSs).

Additional information: Gabbert S, Weikard H-P 2010. A theory of chemicals testing and regulation. Natural Resources Forum 34 (2): 155-164; Gabbert S, Van Ierland EC 2010. Cost-effectiveness analysis of chemical testing for decision-support: How to include animal welfare? Human and Ecological Risk Assessment 16 (3): 603-620

OSIRIS Results Highlights

Database on *in vivo* micronucleus mutagenicity data and analysis of structural alerts (Partners ISS, JRC)

Istituto Superiore di Sanita, Department of Environment and Primary Prevention, Rome, Italy; European Commission's Joint Research Centre, Institute for Health & Consumer Protection, Computational Toxicology Group, Ispra, Italy

The construction of a database on ***in vivo* micronucleus assay data** (**ISSMIC**) has been started, contributing to the Mammalian Toxicity Database developed within OSIRIS.

Data on 150 chemicals tested in the *in vivo* mutagenicity assay has been included in the new database, after critical review of the biological data. The compounds are characterised by structure, CAS, SMILES, chemical name, chemical formula and molecular weight. Data comprise the *in vivo* micronucleus test in male and female mouse and rat in bone marrow, peripheral blood cells and splenocytes.

The data were also used to conduct a study aimed to identify and compile **structural alerts** for *in vivo* micronucleus in rodents. As *in vivo* genotoxicity studies, shortly followed by carcinogenicity studies, are posing a **high demand for animal test resources** and in particular the micronucleus test in rodents is widely used to verify positive *in vitro* mutagenicity tests, estimation techniques such as qualitative or quantitative structure activity relationships (QSARs), read-across and grouping of chemicals might have a huge **saving potential** for the mutagenicity endpoint.

In addition, analyses on the performance of the micronucleus assay confirmed the recognised limitation of the sensitivity of the *in vivo* assay, indicating that its use as screening tool for carcinogenesis needs improvement.

The structural alerts have been implemented as computerised rule of the expert system Toxtree, which is freely available at http://ecb.jrc.ec.europa.eu/qsar/qsar-tools/index.php?c=TOXTREE, and present a tool for preliminary screening of potentially *in vivo* mutagens.

Additional information: Benigni R, Bossa C, Worth A 2010. Structural analysis and predictive value of the rodent *in vivo* micronucleus assay results. Mutagenesis 25 (4): 335-341

A Bayesian network approach to Integrated Testing Strategies (Partners P&G, WUR, RIVM)

Procter & Gamble, Modeling & Simulation Biological Systems, Brussels, Belgium; Wageningen University, Environmental Economics and Natural Resources Group, The Netherlands; National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

The European chemicals legislation REACH establishes a new policy framework for more comprehensive, transparent and efficient data acquisition for chemical risk assessment and management. Integrated Testing Strategies (ITSs), i.e. combinations of different testing and non-testing methods, are expected to be a more efficient approach compared to tiered testing strategies. While ITSs have been proposed for several endpoints, the development of ITSs lacks a methodologically consistent **operational framework** for handling **inference based on multiple evidences**, and allowing optimising testing schemes. Thus, formal approaches of **Weight of Evidence** (WoE) for data integration are needed.

Conceptual requirements for a decision theoretic operational framework are:

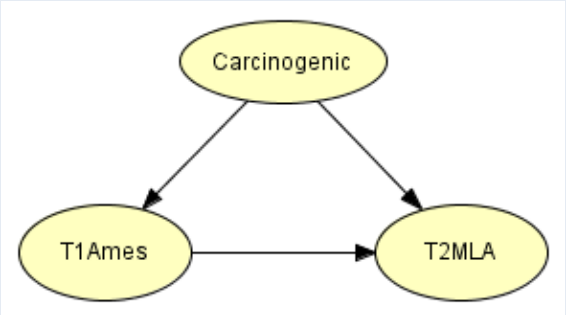
- it should be probabilistic to quantify uncertainty in a formal way
- it should be hypothesis driven and rely on causal relationships
- it should be rational to obtain objective inference.

OSIRIS Results Highlights

An operational framework for quantitative WoE has been developed that uses **Bayesian networks** as the probabilistic framework for data integration and inference.

Bayesian inference uses a numerical estimate, i.e. probability, of the degree of belief in a hypothesis before evidence has been observed and calculates a numerical estimate of the degree of belief in the hypothesis after evidence has been observed. The **degree of belief in a hypothesis** generally changes with accumulating evidence. This process may be repeated with any additional evidence obtained.

The Bayesian network approach has been illustrated for a **two-test battery for carcinogenicity assessment**, using two *in vitro* genotoxicity tests, the Ames test and the Mouse Lymphoma Assay (MLA). The two-test Bayesian network was implemented in a spreadsheet in order to calculate the posterior predictive values for different test results. The analysis started from the observed cell counts of carcinogens and non-carcinogens, which were subjected to both tests. The Bayesian probabilistic inference framework developed proved to be a conceptually consistent and analytically powerful tool for achieving correct inference as a **pre-requisite for ITS development and optimisation**.



Bayesian network for the two-test battery. The arrows describe probabilistic causality quantified by conditional probabilities.

(Figure from Jaworska J, Gabbert S, Aldenberg T 2010 Regul. Toxicol. Pharmacol. 57: 157-167)

Additional information: Jaworska J, Gabbert S, Aldenberg T 2010. Towards optimization of chemical testing under REACH: A Bayesian network approach to Integrated Testing Strategies. Regul. Toxicol. Pharmacol. 57 (2-3): 157-167

Final OSIRIS Meeting

The Final OSIRIS Meeting will be held

on 27 – 29 September 2011

in Leipzig, Germany,

at the Helmholtz Centre for Environmental Research – UFZ, hosted by the OSIRIS Coordinator UFZ.

Photo: Andrea Richarz

The Final Meeting will include the final OSIRIS General Assembly meeting and the final dissemination event:

The results obtained within OSIRIS will be presented and the final version of the OSIRIS Integrated Testing Strategies (ITS) web tool will be demonstrated to Stakeholders.

New OSIRIS Publications

Publications in Peer Reviewed Scientific Journals

- Smith KEC, Dom N, Blust R, Mayer P 2010. Controlling and maintaining exposure of hydrophobic organic compounds in aquatic toxicity tests by passive dosing. Aquat. Toxicol. 98 (1): 15-24
- Hewitt M, Ellison CM, Enoch SJ, Madden JC, Cronin MTD 2010. Integrating (Q)SAR, expert system and read-across approaches for the prediction of developmental toxicity. Reprod. Toxicol. 30 (1): 147-160
- Franco A, Trapp S 2010. A multimedia activity model for ionizable chemicals: validation study with 2,4-dichlorophenoxyacetic acid, aniline and trimethoprim. Environ. Toxicol. Chem. 29 (4): 789–799
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The publication list with **links to the articles** is also available at **www.osiris-reach.eu** > OSIRIS Publications

Conference Calendar: OSIRIS-related Events

Predictive ADMET Workshop
2 – 6 August 2010, Oxford, UK
Application of Predictive ADME and Toxicology methods to case studies, a Hands-on 5 Day eCheminfo Workshop Week
http://echeminfo.com/COMTY_oxfordadmet10

3rd EuCheMS Chemistry Congress
29 August – 2 September 2010, Nürnberg, Germany
European Association for Chemical and Molecular Sciences
http://www.euchems-congress2010.org/ecc.htm

2nd Annual Predictive Toxicology
2 – 3 September 2010, Berlin, Germany
http://www.melifesciences.com/PreTox

16th Congress on Alternatives to Animal Testing – Linz 2010
16th International Congress on In Vitro Toxicology – ESTIV 2010
2 – 4 September 2010, Linz, Austria
EUSAAT - European Society for Alternatives to Animal Testing, ESTIV - European Society of Toxicology in vitro, zet - Austrian Centre for Alternative and Complementary Methods to Animal Testing
http://www.eusaat.org/index.php/2010

Joint Meeting of the SETAC-GLB and GDCh
6 – 9 September 2010, Dessau, Germany
Society of Environmental Toxicology and Chemistry (SETAC GLB), German Chemical Society (GDCh)
http://www.gdch.de/vas/tagungen/tg/5414.htm

Society of Environmental Toxicology and Chemistry UK Branch Annual Meeting 2010
13 – 14 September 2010, London, UK
Environmental Pollution in a Changing World
Plus SETAC-UK Training Workshop "Risk Assessment of Chemicals" on 15 September 2010
http://www.setac-uk.org.uk/setacEvents.html

Risk Analysis 2010 - 7th International Conference on Computer Simulation in Risk Analysis and Hazard Mitigation
13 – 15 September 2010, Algarve, Portugal
http://www.wessex.ac.uk/10-conferences/risk-analysis-2010-3.html

18th European Symposium on Quantitative Structure-Activity Relationships
19 – 24 September 2010, Rhodes, Greece
http://www.euroqsar2010.gr/

3rd International Symposium "Genotoxicity in aquatic systems: Causes, effects and regulatory needs"
22 – 24 September 2010, Freiburg im Breisgau, Germany
http://www.setac-glb.de/fileadmin/setac/redakteure/Veranstaltungshinweise/Flyer-First_Announcement_Freiburg_2010_22022010.pdf

2nd Lhasa Symposium on New Horizons in Toxicity Prediction
23 – 24 September 2010, Leeds, UK
http://www.lhasasymposium.com/

SETAC North America 31st Annual Meeting
7 – 11 November 2010, Portland, Oregon, USA
http://portland.setac.org/

EMEC11 - 11th European Meeting on Environmental Chemistry
8 – 11 December 2010, Portoroz, Slovenia
http://sabotin.ung.si/~emec11/

SOT 2011 - 50th Society of Toxicology Annual Meeting
6 – 10 March 2011, Washington, D.C., USA
http://www.toxicology.org/AI/MEET/AM2011/index.asp

SETAC Europe 21st Annual Meeting
15 – 19 May 2011, Milan, Italy
http://milano.setac.eu/

8th World Congress on Alternatives & Animal Use in the Life Sciences
21 – 25 August 2011, Montréal, Canada
http://www.wc8.ccac.ca/

EUROTOX 2011
28 – 31 August 2011, Paris, France
http://www.eurotox.com/pag.asp?ID_pagina=68

www.osiris-reach.eu > OSIRIS Events and Activities

Fourth OSIRIS Annual Meeting

The Fourth OSIRIS Annual Meeting will take place

on 9 – 11 March 2011
in Barcelona, Spain,

at the University of Barcelona campus at the Barcelona Science Park.

It will be hosted by the OSIRIS partner Universitat Rovira i Virgili (URV).

Photo: Andrea Richarz

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On the agenda:

- Results of the 4th project year
- Planning for the last months of the project and beyond
- Intra- and inter-Pillar/-Workpackage discussions

OSIRIS Stakeholder Interviews on ITS Acceptance

Integrated Testing Strategies (ITS) are expected to meet information requirements in a quicker and more efficient way, including **less animal use.**

The usefulness of ITS for the REACH process, however, depends on their meeting the **users' needs** and on the **acceptance of the results** by ECHA.

OSIRIS is **investigating stakeholders' views** on

- the definition of ITS
- the scope and limitations of ITS use for hazard and risk assessment of chemicals in the context of REACH, including the valuation of animal welfare
- the challenges and requirements for ensuring or improving ITS acceptance and implementation.

The survey consists of **qualitative phone interviews** and a **questionnaire** addressing the interview questions in more detail.

If you are interested in supporting this investigation on ITS acceptance, please contact:
Christina Benighaus (benighaus@dialogik-expert.de) or **Silke Gabbert (silke.gabbert@wur.nl)**.

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SIXTH FRAMEWORK PROGRAMME