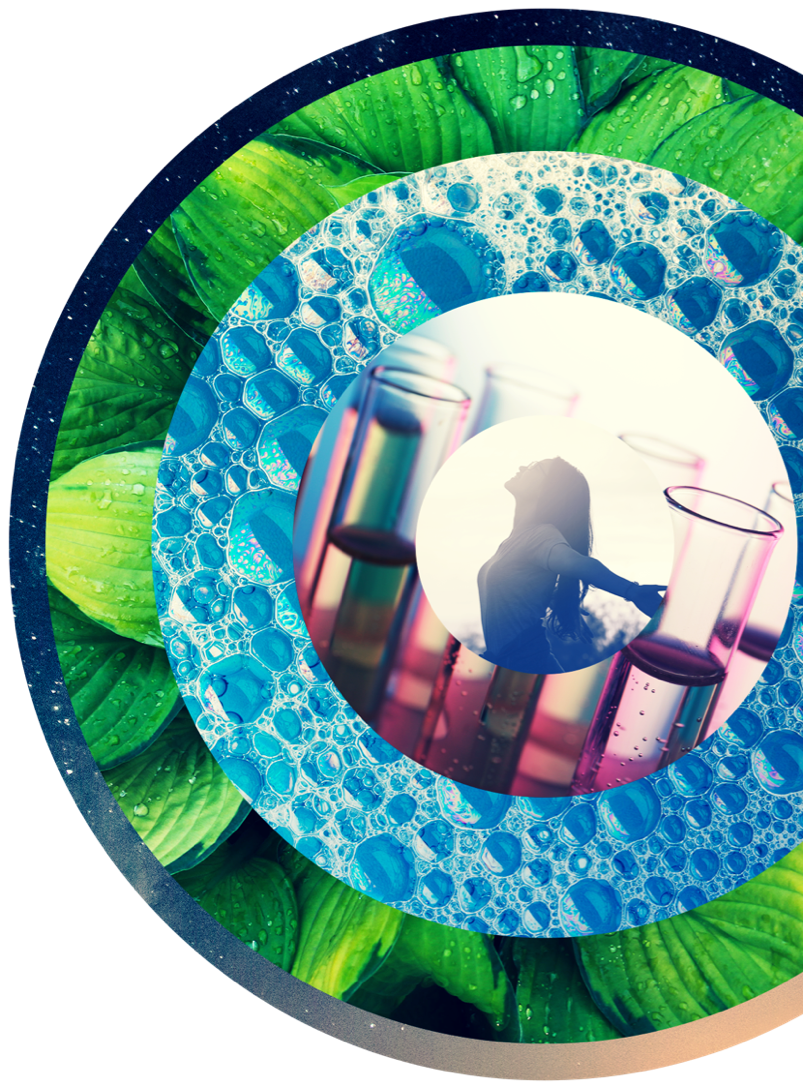
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IN 2021

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AIMT5/5.2 | A developmental ontology based computational model for mammalian neural tube closure for in silico prediction of compound induced neural tube defects

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**Summary**

The objective of this project was to translate the developmental ontology for neural tube closure, which was constructed in the LRI AIMT-5 project, into a computational model for predictive toxicology of neural tube defects. This represents a penultimate step for the proof of principle of this ontology approach towards designing computational solutions to chemical hazard and risk assessment with less reliance on animal testing.

In the LRI AIMT-5 project, we established a novel Developmental Toxicity Ontology (DTO), organizing information about Modes of Action (MoA) and their relationships with Adverse Outcome Pathways (AOPs) in developmental toxicity through an understanding of normal embryology. The DTO integrates MoA and AOP information from three different perspectives, the biological, the chemical and the toxicological perspective focusing on neural tube closure to provide a proof of principle for the ontology approach. The cellular and molecular mechanisms of neural tube closure have been subject of extensive studies, which have allowed us to compile existing information in an ontology framework using a standardized nomenclature that maps the different cell types involved, their morphogenetic functions, and regulatory cytokines and genes underlying their functionalities.

Further challenges for science and technology development remain toward building and testing a fully functional computational platform that can quantitatively predict the probability of a ‘teratological tipping point’ utilizing chemical structure information, in vitro data and in silico models for exposure and hazard.

**Publications**

Yvonne C.M. Staal, Jeroen L.A. Pennings, Ellen V.S. Hessel, and Aldert H. Piersma. [Advanced Toxicological Risk Assessment by Implementation of Ontologies Operationalized in Computational Models](https://www.liebertpub.com/doi/abs/10.1089/aivt.2017.0019). Applied In Vitro Toxicology. Volume: 3 Issue 4: Dec 1, 2017.

Posters:

Yvonne C.M. Staal, Nancy Baker, Lyle D. Burgoon, George Daston, Thomas B. Knudsen, Aldert H. Piersma. [Towards Building an AOP-based Prenatal Developmental Toxicity Ontology](http://cefic-lri.org/wp-content/uploads/2016/02/DEVONT-at-CEFIC-LRI-nov2016.pdf). Cefic-LRI 18th Annual Workshop, November 2016, Brussels, Belgium.

Yvonne C.M. Staal, Nancy Baker, Lyle D. Burgoon, George Daston, Thomas B. Knudsen, Aldert H. Piersma. [An AOP-based Ontology for Neural Tube Closure Caused by Disturbance in Retinoic Acid Signaling](http://cefic-lri.org/wp-content/uploads/2016/02/DEVONT-at-EUROTOX-sept2018.pdf). EUROTOX, September 2018, Brussels, Belgium.

Yvonne C.M. Staal, Nancy Baker, Lyle D. Burgoon, George Daston, Thomas B. Knudsen, Aldert H. Piersma. [Developmental Ontology: Computational modeling of Retinoic Acid in Development of Spina Bifida](http://cefic-lri.org/wp-content/uploads/2016/02/DEVONT-at-SOT-march2017.pdf). Society of Toxicology 56th Annual Meeting, Baltimore, Maryland, USA.

AIMT10 | Development and testing of a repeated dose toxicity ontology model for chemical risk assessment purposes: liver effects as a case study

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**Summary**

The aim of this study was to build a map of the cellular processes and their interactions underlying the closure of the neural tube in vertebrates, and to translate this map into a computational model that can be used as a tool to predict the effects of chemicals on neural tube closure. In the process of neural tube closure, cellular behavior is governed by specific gene expression patterns, that drive cell proliferation, differentiation and interactions in a spatially strictly defined matter. In the neural plate stage, six cell types were defined with their specific gene expressions, the cytokines they produce and the cell behaviors they influence. The resulting map is a complete mechanistic description of the biology underlying neural tube closure. In parallel, a 3D computational model was developed describing the elevation of the neural plate to a semi-tube. The full closure could not yet be modelled within the time frame of the project. This was caused by the realization during the project that the anticipated 2D closure model would neglect some essential features of neural tube closure. The 3D approach that was then followed was logically of a much higher complexity and therefore required more computing time than available within the project. The next step will be the completion of the computational model, followed by functionally linking the computational model with the biological map, so that the computational process is virtually governed by the biological mechanisms. Once that has been achieved, it will be possible to feed data from compound-induced gene expression changes observed in simple in vitro cell systems into the computational model, which will then predict effects at the level of neural tube formation. Thus, the combination of simple in vitro assays with the computational model that integrates data at the level of the embryo will provide an animal-free approach to chemical hazard assessment. It is expected that computational approaches supported by in vitro assays will increasingly be used for chemical hazard assessment. It offers opportunities to avoid animal testing, to fine-tune hazard assessment to human physiology, and allow for mechanistic understanding of chemical toxicity, providing a better informed basis for risk assessment.

**Publications**

Tabernilla, A., dos Santos Rodrigues, B., Pieters, A., Caufriez, A., Leroy, K., Van Campenhout, R., Cooreman, A., Gomes, A.R., Arnesdotter, E., Gijbels, E. and Vinken, M., 2021. In Vitro Liver Toxicity Testing of Chemicals: A Pragmatic Approach. International Journal of Molecular Sciences, 22(9), p.5038.

Gijbels, E., Devisscher, L. and Vinken, M., 2021. Testing in vitro tools for the prediction of cholestatic liver injury induced by non-pharmaceutical chemicals. Food and Chemical Toxicology, 152, p.112165.

Firman, J.W., Pestana, C.B., Rathman, J.F., Vinken, M., Yang, C. and Cronin, M.T., 2020. A Robust, Mechanistically Based In Silico Structural Profiler for Hepatic Cholestasis. *Chemical Research in Toxicology*.

Gustafson, E., Debruyne, C., De Troyer, O., Rogiers, V., Vinken, M. and Vanhaecke, T., 2020. Screening of repeated dose toxicity data in safety evaluation reports of cosmetic ingredients issued by the Scientific Committee on Consumer Safety between 2009 and 2019. *Archives of Toxicology*, *94*(11), pp.3723-3735.

**Timeline and LRI funding**

3 years: from April 1st 2018 to March 30th 2021

€ 906 386 (Year 1: 150kEur Cefic LRI + 150kEur CE ; Year2-3 : 600kEur CE)

B15.2/15.3 | DEVELOPMENT OF AN INTEGRATED RISK MANAGEMENT MEASURE LIBRARY/ ECEL V3.0: TECHNICAL IMPROVEMENTS AND POPULATION OF THE INTEGRATED RISK MANAGEMENT MEASURE (RMM) LIBRARY

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**Summary**

The main goal of the CEFIC LRI B15 project was to develop a well-designed and user-friendly tool with up-to-date information that is supportive to industry for a wide range of Risk Management Measure (RMM) applications. This information is required in the context of the European Chemicals policy (REACH - Registration, Evaluation and Authorization of Chemicals) and other European regulations to demonstrate and document safe use of substances based on quantitative exposures and exposure reduction by Risk Management Measures (RMM). The CEFIC LRI B15 project was therefore intended to support guidance documents from the European Chemicals Agency (ECHA) and to compile REACH registration dossiers. To achieve this goal, TNO developed ECEL v3.0 - an Integrated Risk Management Measure (RMM) library as part of the CEFIC LRI B15 project. The key objectives were twofold: (1) to develop a webbased user-friendly and stable database structure with functionalities that are suitable to search for relevant information on RMM, (2) to populate the library with up-to-date information on RMM for both occupational and environmental settings. Two user groups were targeted. First, registrant users who wish to evaluate the quantitative effectiveness of a specific RMM for registration purposes, and secondly downstream users (industry, research, consulting) who require information on the most suitable or optimal RMM by evaluating different types of control systems and their effectiveness for an exposure or emission scenario. The project was conducted in two parts and in line with the objectives (technical development and data population) and executed in tandem. The 1 st part involved the building of a database structure in a stable IT environment. The TNO DIAMONDS platform (https://diamonds.tno.nl/) was chosen for this purpose. The library was designed to accommodate two separate modules: occupational and environment. Some important aspects of the technical development were the development of an intuitive user interface, the inclusion of functionalities for fit-for-purpose searching & saving of data, the uploading of RMM data and testing of the tool. The 2nd part consisted of the data population of the database. For both the occupational and environmental modules, a systematic literature review (2012-2020) was performed with an abstract screening tool in the DIAMONDS platform. Using a structured approach and screening criteria, suitable data was evaluated, extracted and entered into the database. One of the criteria applied was that it should be possible to derive a quantitative effectiveness value (% reduction in exposure or concentration) for a RMM from the study in question. Besides the data obtained from the peer reviewed literature and grey literature (case studies, etc.), data was also extracted from various existing (open-source) datasets and databases (3300 records, while >1100 records are available in the environmental module. Besides the new B15-3 literature review conducted in 2019/2020, additional datasets and databases were coded and uploaded in ECEL. For the occupational module, previously entered data from ECEL v1.0 and v2.0 (engineering controls) were included, as well as nano-specific, pesticide and RMM manufacturers’ data. The environmental module also reviewed and uploaded sources such as the IPPC BREF documents and LUSS. ECEL v3.0 therefore integrates a broad spectrum of data and includes a wide range of RMM applications in different industrial settings. However, the data available for different types of RMMs remain highly variable. For example, in the occupational module, a considerable number of records are available for local exhaust ventilations systems (LEV) with 1246 records (360 studies), whereas suppression techniques gives 266 records (62 studies) and for product / substance control only 52 records (8 studies) are available. Although the overall number of available records are promising, the availability of sufficient reliable RMM effectiveness data for some less known RMM types are either limited or not available. It was concluded in this project that, despite the current data gaps in RMM effectiveness, ECEL v3.0 offers a comprehensive source of information. It combines the data with a user-friendly interface and ample functionalities to search for relevant data. It is envisaged that this open-source database will be beneficial to both registrants and downstream users, and it is our mission to promote ECEL to all relevant stakeholders and to motivate industry and researchers to share RMM effectiveness data and work together to expand on the ECEL database in the future.

**Publications**

Henk Goede, Remy Franken, Eugene van Someren, Wouter Fransman, Rianda Gerritsen-Ebben. [CEFIC LRI B15-2: Development of an integrated risk management measure library](http://cefic-lri.org/wp-content/uploads/2018/05/Poster-CEFIC-LRI-B15-2_finalx.pdf). Cefic-LRI 19th Annual Workshop, November 2017, Brussels, Belgium.

Henk Goede, Remy Franken, Eugene van Someren, Wouter Fransman, Rianda Gerritsen-Ebben. [Development of an integrated risk management measure library](http://cefic-lri.org/wp-content/uploads/2018/05/18-9942-A0-poster-ECEL-2.pdf). ISES Europe Workshop, June 2018, Dortmund, Germany.

TNO report TNO2018 R10786 LRI B 15.2 TNO: Development of an integrated risk management measure library Date 18 September 2018 Author(s) H.A. Goede R.M. van Stokkum R.A. Franken E.P. van Someren J.T.W.E. Vogels J.E.M Polman G. Kalkman M.G. Gerritsen-Ebben Wouter Fransman (see attached)

The database itself including user manual Diamonds 3 (tno.nl)and no report but an executive summary: Press release: <https://www.tno.nl/en/about-tno/news/2020/10/tno-launches-risk-management-measures-library/>

**Timeline and LRI funding**

B15.2: June 2018 - January 2019

€ 64 000

B15.3: September 2019 - April 2020

€ 157 689

C4 | TRANSCRIPTOMICS BIOINFORMATICS BEST PRACTICES IN TOXICOGENOMICS FOR REGULATORY APPLICATION

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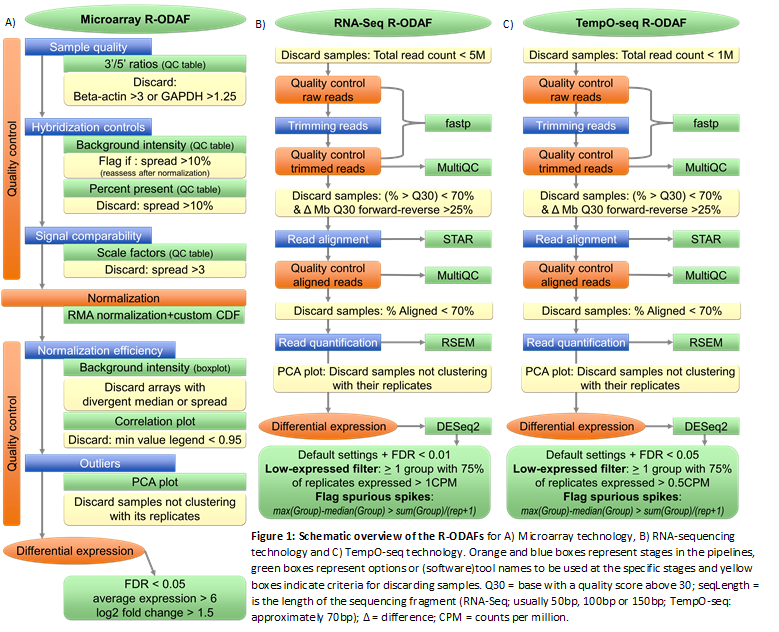
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Summary

The use of various omics techniques for scientific research is increasing. While toxicogenomics studies have already produced substantial data on diverse omics platforms, and despite the promises and excitement of 20 years ago when it was widely speculated that omics methods would reduce or even replace animal use and allow an enhanced understanding of hazard and susceptibility , to date there has been little routine application in regulatory toxicology. One of the reasons for this has been a trepidation about relying on the produced data. It has been argued that omics outputs might not be sufficiently reliable for regulatory application because the techniques, bioinformatics and interpretation can vary. For these reasons, the robustness of the obtained results is questioned. This reticence to trust omics data is further magnified by the lack of internationally agreed upon guidelines and protocols for both the generation and processing of omics data.

This C4 LRI project was established with the ambition to propose for the regulatory community an omics data analysis framework (R-ODAF) for the main transcriptomics platform available on the market: microarrays, RNA-sequencing or TempO-seq sequencing technologies. For this, in the first phase of the project, datasets of the three selected platforms were accumulated, and a complete review of all used data analysis pipeline were performed. After selecting of the most relevant tools and algorithms for each platform, the second phase of the project consisted in evaluating all possible parameters and design three individual ODAF. The quality and reproducibility of the output was of course a primordial criterion for the selection of the pipeline, together with the accessibility of the tools, the user-friendliness, and the interoperability of the final product. In a final phase, the three different proposed ODAFs were assessed with several dataset to evaluate the efficiency of the proposed pipeline in calling a list of differentially expressed genes as accurately as possible.

The final R-ODAF is then composed of three individual pipelines for microarray, RNA-Sequencing and TempO-Seq platform, as summarize in figure 1:



Publications

1. Verheijen M, Tong W, Shi L, Gqnt TW, Seligmann B, Caiment F. 2020. Birch H, Kramer NI, Mayer P. 2019. Towards the development of an omics data analysis framework. Regul Toxicol Pharmacol Volume 112

A second manuscript presenting the final R-ODAF product is in preparation and will be submitted in the near future.

F. Caiment. Towards the development of an omics data analysis framework for regulatory application. MAQC Society 2nd Annual Meeting, February 2018, Shangai, China.

**Timeline and LRI funding**

April 2018 - April 2020

€ 250 000

ECO 37 | D-BASS – DEVELOPING A BIOACCUMULATION ASSESSMENT STRATEGY FOR SURFACTANTS

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**Summary**

The BIONIC v3 model was developed allowing the user to enter an organic carbon-water partition coefficient or distribution ratio (KOC or DOC respectively) and the estimated total organic carbon level in the test system (mg TOC/L). One of the key actions was to refine the Tier for Surfactants and to refine the BCF assessment scheme as presented in Figure 1.

Using the two inputs, BIONIC v3 calculates the estimated freely-dissolved fraction of the chemical in the aqueous phase of the test system and generates predicted BCFs referenced to total water concentration and freely-dissolved concentration and displays these outputs for the user. It calculates uses the measured in vitro clearances as input and extrapolated them to whole body biotransformation rate constants (IVIVE). The BIONIC v3 model addresses pH dependence by allowing the user to specify the bulk water and gill pH as part of the model parameterization; predicted BCFs for cationic surfactants do increase with greater bulk water (and gill) pH.



Figure 1. The revised scheme (from Milestone D16 report (version 2020-12-09).

The user can enter mucus-water partitioning data as part of the model parameterization which is then used to calculate a “BCF w/ surface sorption” based on the estimated surface area of the fish, where surface area of the fish is estimated from size (kg).

BIONIC v3 generates model output with and without considering surface sorption; if mucus-water partitioning data are entered by the user, the predicted BCFs with surface sorption are always greater than predicted BCFs excluding the contribution (i.e., more conservative).

The BIONIC model performance for anionic vs. cationic surfactants – The performance of the BIONIC v3 model for anionic surfactants (conservative/small overprediction of BCF when including in vitro biotransformation data) is consistent with expectations and observations for neutral organics; the performance for cationics (not conservative/underprediction of BCF when including in vitro biotransformation data) is noteworthy.

**Publications**

Droge S, McLachlan MS, Arnot JA, Armitage JM. EXECUTIVE SUMMARY – “CEFIC LRI-ECO37 – D-BASS: Development of a bioaccumulation assessment strategy for surfactants”, November 2020.

Droge STG. Membrane–Water Partition Coefficients to Aid Risk Assessment of Perfluoroalkyl Anions and Alkyl Sulfates. Environ. Sci. Technol. 2018 Dec 20.

Kierkegaard A, Chen C, Armitage JM, Arnot JA, Droge S, McLachlan MS. Tissue Distribution of Several Series of Cationic Surfactants in Rainbow Trout (Oncorhynchus mykiss) Following Exposure via Water. Environ Sci Technol. 2020 Mar 18.

Kierkegaard, A., Chen, C.E., Armitage, J.M., Arnot, J.A., Droge, S. and McLachlan, M.S., 2020. Tissue distribution of several series of cationic surfactants in rainbow trout (Oncorhynchus mykiss) following exposure via water. Environmental science & technology, 54(7), pp.4190-4199.

Droge, Steven; Armitage, James; Arnot, Jon; Fitzsimmons, Patrick; Nichols, John. Biotransformation potential of cationic surfactants in fish assessed with rainbow trout liver S9 fractions. Environmental Toxicology and Chemistry Manuscript judged as needing revision (deadline August 8, 2021).

**Timeline and LRI funding**

March 2017 - August 2019

€ 500 000

ECO 39/39.2 | REVIEW, RING-TEST AND GUIDANCE FOR TKTD MODELLING

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**Summary**

Stressors, such as toxicants, can cause mortality among organisms. Interestingly, not all individuals will die at the same time in the same exposure treatment, and the number of deaths will change with exposure time. The pattern of mortality will also depend on the exposure profile (e.g., constant versus pulsed exposure, fluctuating or time-variable exposure).

Making sense of these issues requires mechanism-based models, known as toxicokinetic-toxicodynamic (TKTD) models. For mortality, almost all published TKTD models can now be viewed as members of an over-arching framework: the General Unified Threshold model of Survival (GUTS). The additional information and insight gained through the application of toxicokinetic-toxicodynamic (TKTD) modelling can strengthen the environmental risk assessment of chemicals in consumer products or plant protection products (PPPs). For the endpoint survival the most suitable and powerful tool is currently the General Unified Threshold model of Survival (GUTS), which consists of two complimentary models: GUTS-SD (stochastic death) and GUTS-IT (individual tolerance).

GUTS has been submitted as part of the environmental risk assessment of PPPs, but it can also be used in the context of REACH. In order to ease the use of GUTS and increase trust and acceptability we recently released an extensive e-book and carried out a ring-test of different implementations of GUTS (ECO39).

The results from CEFIC-LRI ECO39 suggested that we needed a user-friendly, robust, freely-available and open-source software for standard GUTS applications. The ECO39.2 extension produced such a tool.

**Publications**

Publications:

Tjalling Jager & Roman Ashauer. Modelling survival under chemical stress. LeanPub [Ebook](https://leanpub.com/guts_book" \t "_blank), 2018 Jan 18, ISBN 978-1-9999705-0-5.

Tjalling Jager & Roman Ashauer. [How to evaluate the quality of toxicokinetic – toxicodynamic models in the context of environmental risk assessment](https://setac.onlinelibrary.wiley.com/doi/abs/10.1002/ieam.2026). Integr Environ Assess Manag. 2018 Mar 24; 14(5): 604-614.

Roman Ashauer & Tjalling Jager. [Physiological modes of action across species and toxicants: the key to predictive ecotoxicology](http://pubs.rsc.org/en/Content/ArticleLanding/2018/EM/C7EM00328E#!divAbstract). Environ Sci Process Impacts, 2018 Jan 24; 20(1):48-57.

Presentations:

Tjalling Jager. [Applying criteria for model evaluation to TKTD models.](http://cefic-lri.org/wp-content/uploads/2017/02/ECO39_Jager_SETAC_2017_GUTS.pdf) 27th SETAC Europe Conference, May 2017, Brussels, Belgium.

Posters:

Roman Ashauer, Tjalling Jager. [Review, ring-test and guidance for TKTD modelling.](http://cefic-lri.org/wp-content/uploads/2017/02/CEFIC_LRI-2016_ECO39_poster.pdf) 18th Annual CEFIC-LRI Workshop, November 2016, Brussels, Belgium.

Roman Ashauer, Tjalling Jager. [Review, ring-test and guidance for TKTD modelling.](http://cefic-lri.org/wp-content/uploads/2017/02/CEFIC_LRI_ECO39_poster-SETAC.pdf) 27th SETAC Europe Conference, May 2017, Brussels, Belgium.

Tjalling Jager, Roman Ashauer. [Modelling survival under chemical stress. A comprehensive guide to the GUTS framework.](http://cefic-lri.org/wp-content/uploads/2017/02/ECO39-poster_GUTS_ebook-SETAC-2018.pdf) 28th SETAC Europe Conference, May 2018, Rome, Italy.

Roman Ashauer, Tjalling Jager. [Ring-test of different implementations of the General Unified Threshold model of Survival (GUTS)](http://cefic-lri.org/wp-content/uploads/2017/02/ECO39-poster_GUTS_ringtest-SETAC-2018.pdf). 28th SETAC Europe Conference, May 2018, Rome, Italy.

**Timeline and LRI funding**

ECO39 February 2017 > January 2018  
ECO39.2 July 2018 > December 2019

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ECO 40/40.2 | INVESTIGATIONS ON THE BIOCONCENTRATIONS OF XENOBIOTICS IN THE FRESHWATER AMPHIPOD HYALELLA AZTECA AND INTER-LABORATORY COMPARISON OF A NEW BCF TEST PROTOCOL

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**Summary**

The identification and scientific assessment of compounds that bioaccumulate in organisms and biomagnify in food webs are important aspects in the regulation of chemicals in several jurisdictions, such as Regulation (EC) No 1107/2009, the Regulation on classification, labelling and packaging of substances and mixtures, and the Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

Bioaccumulation also plays an important role in terms of evaluating secondary poisoning. To date, the vast majority of research on bioaccumulation has been conducted on aquatic organisms and uptake through the gills. Bioconcentration studies are commonly carried out according to the OECD Test Guideline (TG) 305. However, fish bioaccumulation studies are time consuming, expensive, and use many laboratory animals.  Alternative methods that replace the use of fish for BCF testing would therefore be of value. The bioaccumulation of sediment-associated contaminants by benthic invertebrates can be assessed by using the bioaccumulation tests following technical guidance document OECD 315 (OECD, 2008). However, the test endpoint is defined as a bioaccumulation factor (BAF). A suitable method to deduce BCFs from BAFs derived from OECD 315 studies is still not available leading to a limited value of this test from the regulatory point of view. Bioconcentration data can be obtained by conducting flow-through tests with bivalve mollusks. However, an established test procedure for bioconcentration tests with freshwater bivalves is missing and would be difficult to implement regarding the selection of an appropriate test species on the basis of availability, ecological importance, past successful use, and ease of handling in the laboratory.

*Hyalella azteca* is an epibenthic amphipod which is widespread in North and Middle America and commonly used for ecotoxicity studies with and without sediment (Environment Canada, 2013). Several laboratory studies have been carried out with *H. azteca* to elucidate the bioconcentration potential of metals and organo-metals (e.g.  Shuhaimi-Othman 2007; Norwood et al. 2007; Alves et al. 2009).

Investigations on the toxicokinetics and bioconcentration of organic compounds in *H. azteca* included compounds like chlorinated and polycyclic aromatic hydrocarbons, the insecticide DDT and the synthetic hormone 17α-ethinylestradiol (Lee et al. 2002; Landrum et al. 2004; Nuutinen et al. 2003; Lotufo et al. 2000). The water-only assays were usually carried out under static or semi-static conditions following no standardized protocol. In a recent study a range of compounds of different lipophilicity (log Kow 3.45-7.8) were tested under flow-through conditions. The results showed that bioaccumulation test with *H. azteca* could be an appropriate test to predict no B-vB classification (BCF < 2000) in the standard fish test (Schlechtriem et al. 2015).

Objectives:

The main objective of this project is to develop a validated test protocol for the use of *H. azteca* in aquatic BCF studies. For this, the following specific objectives were addressed:

Phase 1:

* To collate existing information as well as develop new data to compare biotransformation of xenobiotics in *azteca* and fish.
* To assess the usefulness of experimental elimination rate constants as test parameters that we can combine with our mechanistic knowledge on partition and transport processes in aquatic and terrestrial organisms in order to derive BCF and BMF values needed for chemical regulation
* To prepare a detailed test protocol for use of *azteca* in aquatic BCF studies for the ring-test.
* To have regular dialogue with regulatory agencies, such as UBA and ECHA, over the acceptability of *azteca* as an alternative, non-vertebrate test species for bioaccumulation assessment.

Phase 2:

* To organise an inter -laboratory comparison (‘ring -test’) with known test compounds to validate the test protocol (at least six partners).

**Publications:**

Goss KU, Linden L, Ulrich N, Schlechtriem C. [Revisiting elimination half live as an indicator for bioaccumulation in fish and terrestrial mammals](https://www.sciencedirect.com/science/article/pii/S0045653518312748?via%3Dihub). Chemosphere. 2018 Nov;210:341-346.

Conference proceedings:

[The use of toxicokinetic data for assessing bioaccumulation](http://cefic-lri.org/wp-content/uploads/2018/04/UFZ-WS_TK-data-for-assessing-bioaccumulation_Leipzig-21st-Feb-2018_REPORT.pdf), Workshop, Helmholtz Centre for Environmental Research GmbH – UFZ, February 2018, Leipzig, Germany.

**Timeline and LRI funding**

ECO39: February 2017 - January 2019

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ECO 45 | CHEMICALS – ASSESSMENT OF RISKS TO ECOSYSTEM SERVICES (CARES) II

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**Summary**

A multidisciplinary team including ecologists, ecotoxicologists and risk assessors used existing information to undertake a minimum of six environmental risk assessments across three case studies. For each case study, the environmental risk of the study chemical(s) was assessed using both existing regulatory frameworks (e.g. REACH, EC 1107/2009) and an ecosystem service approach. Two case studies focussed on prospective risk assessment and one case study on retrospective risk assessment. Each case study considered multiple ecosystem services and, where appropriate, multiple environmental compartments. Key stakeholders from the chemical industry, regulatory authorities (including risk managers) and academia participated in two events; the first to agree the design of the case studies and the second to evaluate the case study outcomes. The applicability of existing approaches (i.e. test methodologies, indicators, EPFs) for assessing chemical risk to ecosystem service delivery was evaluated prior to undertaking the case studies.

Outputs: Worked examples of tiered risk assessment processes addressing the impacts of chemical exposure on the delivery of multiple ecosystem services. Peer-reviewed manuscripts.

Outcome: Evaluation of the added value to regulatory decision making of adopting an ecosystem service approach to chemical risk assessment.

**Publications**

Poster: *“*[*Chemicals: Assessment of Risks to Ecosystem Services (CARES) II”*](http://cefic-lri.org/wp-content/uploads/2018/04/SE_2020_Surfactant_PoC_poster.pdf), Lorraine Maltby, Paul J. Van den Brink, Jack Faber, Stuart Marshall

Poster: [*“Chemicals: Assessment of Risks to Ecosystem Services (CARES II) – Proof of concept case study on zinc (retrospective ERA)”*](http://cefic-lri.org/wp-content/uploads/2018/04/SE_2020_metal_PoC_poster.pdf), A Ross Brown1, Stuart Marshall2, Chris Cooper3, Paul Whitehouse4, June Jones4, Jonny Griffiths4, Paul Van den Brink5, Jack Faber5 Lorraine Maltby6

Presentation: [*“Assessing chemical risk within an ecosystem services framework: a proof of concept studies”*](http://cefic-lri.org/wp-content/uploads/2018/04/SE_2020_PoC_studies_-platform.pdf), Lorraine Maltby, Paul van den Brink, Jack Faber, Stuart Marshall, Ross Brown

Poster: [*“Environmental risk assessment of plant protection products using the ecosystem services concept: Prospective proof of concept case study”*](http://cefic-lri.org/wp-content/uploads/2018/04/SE_2020_PPP_PoC_poster.pdf), Paul J. Van den Brink, Pernille Thorbek, Nika Galic, Hans Baveco, Annika Agatz, Anne Alix and Lorraine Maltby

Poster: [*“Chemicals: Assessment of Risks to Ecosystem Services (CARES II) – Proof of concept case study of a surfactant used in consumer products”*](http://cefic-lri.org/wp-content/uploads/2018/04/SE_2020_Surfactant_PoC_poster.pdf), Stuart Marshall, Oliver Warwick, Mike Crookes, Nika Galic, Lorraine Maltby, Paul J. Van den Brink, Jack Faber, Ross Brown

**Timeline and LRI funding**

April 2018 - April 2020

€ 400 000