CEFIC Long-range Research Initiative
Request for Proposals (RfP)

RfP (project code LRI-ECO21)

Title:
Mechanistic Bioaccumulation Model(s) for Ionogenic Organic Substances in Fish

Background

Reliable bioconcentration data for fish are a prerequisite for PBT and environmental risk assessment of organic substances. The standard endpoint is a fish bioconcentration factor (BCF) developed using OECD TG 305 (OECD, 2012). The test uses a considerable number of vertebrate animals, is costly, and for certain classes of substances like cationic surfactants, is not applicable due to the inherent substance properties e.g. strong sorption to negatively charged biota.
Mechanistic models addressing the absorption, distribution, metabolism and excretion (ADME) of substances in fish have been developed (Dimitrov et al, 2012; Arnot & Gobas, 2004), and represent alternative methods for estimating bioaccumulation potential in fish. The ADME approach requires sound data on the metabolic rate constant (K_m) in fish (Nichols et al, 2007). Measured K_m are rarely available, and fragment-based estimation methods are used instead (Arnot et al, 2008, Mekenyan et al, 2006). In recent years, in vitro methods for the measurement of fish metabolism rates have been developed (Nichols et al, 2007, LRI Project ECO6.2, 2008) to allow for the inclusion of more realistic data to new and existing predictive models. Minimal data exists for ionogenic organic substances, and as such, these compounds are generally outside of the applicability domain for existing models (e.g. the BCFBAF module of EPISuite). Data is required to allow for the development and inclusion of ionogenic substances in predictive models, including how speciation changes with pH and time, bioavailability in test media, and the influence of sorption in the test systems.

Objectives

- Determine whether available mechanistic bioaccumulation models for fish can be adapted such that they may be used for ionogenic organic compounds
- Evaluate missing and required model parameters, and develop experimental data to fill the identified gaps (e.g. information on speciation and sorption, and measurement of K_M for a training set)
- Develop new model(s) for the estimation of fish BCFs, if available models cannot be used for ionogenic organic substances (cationic, anionic, zwitterionic).
- Validate the model(s) experimentally and establish the applicability domain
- Establish an easy to use implementation of the model (e.g for incorporation into LRI Toolbox (AMBIT)/EPISuite/OECD QSAR toolbox)

The final report shall contain an executive summary (2 pages max), a main part (max. 50 pages) and a detailed bibliography. It is expected that the findings will be developed into a peer reviewed publication, following presentation at a suitable scientific conference.

It is also expected that project output will include an easy to use implementation of the model (e.g for incorporation into LRI Toolbox (AMBIT)/EPISuite/OECD QSAR toolbox). A SOP (Standard Operational Procedure) for measuring model parameters e.g. sorption measurements shall be established as well to allow later Contract research labs to carry out such measurements as well.

Cost and Timing

Start in early 2013, duration 2 years
Budget in the order of €300k

Partnering/Co-funding

Applicants should provide an indication of additional partners and funding opportunities that can be appropriately leveraged as part of their proposal. Partners can include, but are not limited to industry, government/regulatory organizations, research institutes, etc. Statements from potential partners should be included in the proposal package.

References

Arnot & Gobas (2004)	Arnot JA, Gobas FABC, A food web bioaccumulation model for organic chemicals in aquatic ecosystems, Envrion. Toxicol. Chem. 2004, 23, 2343-2355
Arnot et al (2008)	Arnot JA, Mackay D, Bonnell M, Estimating metabolic biotransformation rates in fish from laboratory data, Environ. Toxicol. Chem 2008, 27 (2), 342-351
Dimitrov et al (2012)	Dimitrov S, Dimitrova N, Georgieva D, Vasilev K, Hatfield T, Straka J, Mekenyan O, New developments of the bioconcentration factor base-line model, SAR and QSAR in environmental research (impact factor: 1.68). 01/2012; 23(1-2):17-36. DOI: 10.1080/1062936X.2011.623321
LRI Project ECO6.2 (2008)	Pre-validation of an in vitro fish liver S9 assay to optimize the prediction of bioaccumulation, Ehrhard S, Escher B, Sahi J, Johanning K, Weisbrod A, Dyer S, Bernhard MJ, Sharpe A, Eickhoff C http://www.cefic-lri.org/projects/17/21/ECO6-2-ILSIHESI-Pre-validation-of-an-in-vitro-fish-liver-S9-assay-to-optimize-the-prediction-of-bioaccumulation/?cntnt01template=display_list_test
Mekenyan et al (2006)	Mekenyan O, Dimitrov S, Dimitrova N, Metabolic activation of chemicals: In silico simulation. SAR QSAR Environ Res 2006,17,107–20
Meylan & Howard (1995)	Meylan WM and Howard PH , Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 1995, 84, 83-92
Nichols et al (2007)	Nichols J, Erhardt S, Dyer S, James M, Moore M, Plotzke K, Segner H, Schultz J, Thomas K, Vasiluk L, Weisbrod A, Use of In Vitro Absorption, Distribution, Metabolism,and Excretion (ADME) Data in Bioaccumulation Assessments for Fish, Hum.Ecol. Risk Assess.,2007,13 (6) 1164-1191
OECD (2012)	Draft Test Guideline 305, Bioaccumulation in Fish: Aqueous and Dietary Exposure, 2012-03-13, this revision will replace the current version of the Guideline from 1996-06-14

DEADLINE FOR SUBMISSIONS: August 31, 2012
Please see www.cefic-lri.org for the project proposal form and further guidance for grant applications.