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

Title and Code Number: Fate-directed Toxicity Testing and Risk Assessment of UVCBs – **LRI ECO42**

Background

Environmental toxicity information serves two roles in the assessment of a substance for environmental safety and regulatory requirements. The data are used to assess ecotoxicity but also to derive Predicted No-effect Concentrations (PNECs) for environmental risk assessment. In the context of fate and exposure assessment, substance properties (e.g. vapour pressure, water solubility, log K_{ow}, log K_{oc}) and information on biodegradation are needed to estimate the distribution of releases in environmental compartments and to calculate Predicted Environmental Concentrations (PECs) for each compartment. For conventional risk assessment of single substances, these PECs would be compared to PNECs based on aquatic toxicity testing. This process is relatively well established for single chemicals, well-defined substances and simple mixtures.

Multi-constituent substances (MCSs) and substances of unknown or variable composition, complex reaction products or biological materials (UVCBs) pose particular challenges for conventional hazard and risk assessment (see ECHA Guidance for identification and naming of substances under REACH and CLP for more detail). UVCB substances are comprised of individual constituents, each of which may possess different physico-chemical and fate properties. Of 11,998 registered substances in REACH, 10% are multi-constituent and 21% are UVCBs (ECHA Read-Across Assessment Framework), which includes petroleum substances, fragrances/essential oils, pine resins, and surfactants. Risk assessment for multi-constituent substances is hampered by the fact that toxic effects of complex substances cannot be linked to specific constituents; standard guidelines for risk assessment of single chemicals are therefore not applicable. It is known that UVCB substances cannot be sufficiently identified by their chemical composition, which creates the complications for testing using standard guideline methodologies. In addition, the risk assessment of such substances as traditional hazard and exposure assessments for the whole substance, in most cases is not possible. Furthermore, fate and hazard of the different constituents in the environment will be determined by their specific physicochemical properties, but the Unknown and potentially Variable composition of these substances adds a level of uncertainty which is difficult to address by both producers and regulators.

The recent RIFM/ECETOC UVCB Workshop (02-04 November 2016, Florida, USA) highlighted the need to account for complex substance exposure and fate in order to perform more relevant toxicity testing, and raised questions on the impact this type of testing would have on risk assessment outcomes (Salvito and Galay-Burgos, 2017). Aquatic toxicity data for UVCBs can be generated from testing known individual components or testing water accommodated fractions (WAFs) generated from the whole substance. In order to quantify toxicity for classification purposes, the WAF method was developed, although data are considered of limited value for whole substance risk characterisation. In order to lower this uncertainty, a coupled fate and effects approach is envisioned, where the biodegradation of a complex substance is investigated and subsequently toxicity testing is performed on the remaining sample/constituents. In this way, fate of constituents is accounted for by design, thereby increasing the environmental relevance of toxicity testing. Within the Workshop, the attendees, including the regulatory authorities (i.e., ECHA, ECCC, USEPA), were interested in developing this approach, including the development of data/case studies to support its future use.

Objectives

This project is looking to compare hazard and risk assessment outcomes for UVCBs/MCS when using fate-directed versus conventional testing approaches.
Proposals should include development of conceptual, modelling, and analytical techniques to support general purpose environmental risk assessment of UVCBs/MCS. Appropriate, state-of-the-art characterisation techniques, such as GCxGC and LC-MS, can be used to track biodegradation of UVCBs/MCS and component degradants. By developing the appropriate analytical tools coupled to a persistence test, half-lives for fractions of the substance can potentially be estimated. Advanced analytical techniques can also be used to estimate physicochemical properties of the UVCBs/MCS constituents to support existing risk assessment approaches (Nabi and Arey, 2017), as well as modelling hazard properties (e.g., PETROTOX (Redman *et al.*, 2012), using log K_{ow} to model bioaccumulation). Changes in measured physicochemical properties during the biodegradation process may, through modelling, indicate changes to hazard properties, which can then be compared against actual test results.

The project's objectives are to:

1. Develop methods for fate-directed ecotoxicity assessment of UVCBs/MCS, possibly as a tiered approach, to increase environmental realism and decrease conservatism in hazard and risk assessment.
2. Generate case studies on how fate-directed approaches affect the fate, hazard, and risk assessment of a substance compared to more conventional risk assessments based on key constituents or WAF testing.

Scope

1. Literature review on fate-driven toxicity approaches.
2. Identification of potential test substances and/or proposed synthetic mixtures (to be comprised of industry-relevant UVCB/MCS) for the case studies.
3. Address the setup of the biodegradation testing and accompanying analytical techniques. The analysis of the composition of UVCBs/MCS before, during and after biodegradation testing should include approaches to identify and handle minor/unidentified portions of the UVCBs/MCS.
4. Determine the toxicity of the UVCBs/MCS at those different time points/degrees of biodegradation, via data gathering, modelling, or testing to refine the calculation of the PNECs.

5. Consider how you would improve exposure modelling for UVCBs/MCS, and thus improve PEC calculation, based on the biodegradation information and evolving physicochemical properties from the fate-directed studies.
6. Compare the outcomes of resulting risk assessments when using fate-directed approaches versus conventional approaches, which may include WAFs or whole effluent testing.
7. Make recommendations for fate-directed risk assessment of UVCBs/MCS.

Deliverables

Two major outcomes are envisioned:

1) Develop an approach for fate-directed toxicity testing and risk assessment of UVCBs
    - Including a tiered approach to ecotoxicity assessment (exploring the utility of existing methods, and developing new approaches to ecotoxicity assessment) and recommending analytical and methodological tools
    - Develop or improve upon exposure modelling for the determination of PECs based on the outcomes of the fate experiments
2) Comparison of risk assessments using the various approaches, leading to an integrated testing strategy
    - This should include the development of a tiered risk assessment methodology starting with a conservative determination based on UVCB components or blocks of PNECs and PECs without the advantage of the new fate directed approach, through to the application, at the highest tier, of a more robust approach based on the experimental design and recommendations.

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 at least one peer reviewed publication, following poster(s) and presentation(s) at suitable scientific conference(s).

Cost and Timing
Start in January 2018
Duration 3 years
Budget in the order of €450K.

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.

Fit with LRI objectives/Possible regulatory and policy impact involvements/ Dissemination

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

Applicants should provide information on the fit of their proposal with LRI objectives and an indication on how and where they could play a role in the regulatory and policy areas. Dissemination plans should also be laid down.

References

Nabi, D and Arey, JS. Predicting Partitioning and Diffusion Properties of Nonpolar Chemicals in Biotic Media and Passive Sampler Phases by GC × GC. *Environmental Science & Technology* 2017 51 (5), 3001-3011.

Redman, AD, Parkerton, TF, McGrath, JA, Di Toro, DM. PETROTOX: an aquatic toxicity model for petroleum substances. *Environ Toxicol Chem*. 2012 Nov; 31(11):2498-506.

Salvito, D.T. and Galay-Burgos, M. ECETOC/RIFM WS: Developing a strategy to improve the environmental risk assessment of difficult to test multi-component substances Part 1: Background. SETAC North America 37th Annual Meeting, Orlando 2017.

DEADLINE FOR SUBMISSIONS: 31 August 2017

Please see www.cefic-lri.org for general LRI objectives information, project proposal form and further guidance for grant applications.