2017 HESI Emerging Issues Proposal:

Improving fate and ecotoxicity assessment tools to advance the ecological risk assessment of difficult to test multi-component substances

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Is this proposal submitted on behalf of more than one person / institution? If yes, identify co-submitters below. Dan Salvito (RIFM); Miriam Leon-Paumen (ExxonMobil); Karen Jenner (Givaudan)

Proposal title: Improving fate and ecotoxicity assessment tools to advance the ecological risk assessment of difficult to test multi-component substances

Key words: Environmental Risk Assessment, Difficult to Test Substances, UVCBs

Describe the problem to be addressed. Why is the issue important? To whom is this issue important?

Multi-constituent and UVCB substances are comprised of individual constituents which may possess different physico-chemical and fate properties, meaning that the environmental risk assessment should ideally be based on a constituent approach, i.e., either based on groups of constituents with similar environmental fate and toxicity properties or on individual constituents that contribute most to the potential hazard and risk of the mixture. This approach is challenging for substances that are not well-characterised and/or have a significant fraction of "unknown" constituents.

International regulatory frameworks (specifically REACH, Canada's DSL Categorization and Chemicals Management Plan assessments, and USEPA's Premanufacturing Notification (PMN) process) have highlighted the complexities of registering, characterizing fate, exposure, hazard and ultimately assessing the risk of complex chemical mixtures, whether from manufacturing environments or plant-derived materials. Several industrial sectors (e.g., petrochemicals, personal care products, resins/rosins) have developed frameworks and methodologies for characterization and analysis of these complex substances. An international workshop was held on 2 – 4 November 2016 prior to the SETAC World Congress in Orlando, FL to address risk assessment challenges for complex mixtures of substances (e.g., multi-constituent substances (MCSs), substances of unknown or variable composition, complex reaction products or biological materials (UVCBs)). Participants included experts from academia, industry, and government regulatory authorities. This workshop was designed to identify best practices and key research needs to support environmental risk assessment. This issue is important to the global regulatory community and the chemicals industry.

The workshop explored whether standard tests used to generate environmental hazard and fate information for single substances might be appropriate for testing UVCBs and MCSs; how such systems might be modified to provide information on the individual constituents / blocks of constituents and what the relevance of the output data is for environmental risk assessment. Workshop output identified several key needs, one of which included the need for a standing project committee to work on addressing critical issues.

Describe the basic project steps or stages to the best of your ability, including an expected timeline, milestones, and deliverables for the first two years.

In the context of fate and exposure assessment, substance properties (e.g. vapour pressure, water solubility, log Kow, Log Koc) 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. To assess the ability of a chemical to accumulate in organisms via the food chain, information on bioaccumulation is also required.

Determining the biodegradation of mixtures using, among other techniques, analytical monitoring to assess the individual constituents and blocks of constituents is a major challenge. Furthermore, consideration of mixture effects, such as co-metabolism and competitive effects, may be necessary to determine how and if these effects may influence the results of a laboratory study and the interpretation of a UVCB's persistence in the environment.

Environmental toxicity information serves two roles in the assessment of a material for environmental safety and regulatory requirements. The data, in and of itself, are used to assess ecotoxicity, but are also used to derive PNECs for environmental risk assessment. Aquatic toxicity data can be generated from known individual components or from the whole substance by preparing water accomodated fractions. UVCBs present unique challenges in their testing and interpretation of the data generated in standard studies.

As an outcome of the Workshop described above, there is a need to build a tripartite 'community of practice'. Thus far this ad-hoc working group, has identified several areas for future development including, but not limited to:

1. Advancing the methodology and applicability of the Water Accommodated Fraction for determining the ecotoxicity of UVCBs and MCSs.

2. Applicability of Weight of Evidence methodologies for fate and toxicity endpoints used in environmental risk assessments

3. The use of passive dosing methodologies for persistence testing

A HESI group would work to develop solutions for the issues noted above, as well as provide a continuous platform for multi-sector dialogue, a need that is currently not met. The large stakeholder group that has already been established would help to focus these efforts

Specific deliverables, within a two-year horizon, include collaborative research projects (e.g., with RIFM or CEFIC- LRI). Both of these organizations have shown a commitment to this issue and may have significant research funding with which to advance key scientific gaps, which would complement the work of this initiative. Consensus-driven best practices on risk assessment methodologies for UVCBs and MCSs, with communication via peer-review publications are the ultimate goal. Continuation and success of this working group (comprised of members from ECHA, ECCC, USEPA, OECD, RIVM, HESI, RIFM, Givaudan, ExxonMobil, BASF, University of Amsterdam, and Stockholm University) necessitates movement from an ad-hoc working environment to a program-based 'home' that can be provided within HESI's working framework. This would facilitate the achievement, in the very near term and beyond, the development of a working risk assessment framework and a robust research agenda to be funded collaboratively.

What is the potential or anticipated impact of successfully achieving the milestones described above? *(Describe scientific, regulatory, policy, public health, and/or other impacts.)*

Currently, the ecological risk assessment of UVCBs and MCSs presents a significant challenge for industry in identifying and executing appropriate test methodologies for these difficult to study substances, and the regulatory community in interpreting and weighing the data provided. Global regulatory regions are either in the midst of assessing these substances (e.g. EU under REACH, ECCC with its Chemical Categorization program under DSL) or are developing their regulatory paradigms. There are challenges to meeting requirements for these substances in multiple regions, while the science itself is evolving. Strategies to integrate relevant information, new scientific methods, and exposure and hazard information are needed, along with characterization of associated uncertainty and variability.

Describe the interdisciplinary, collaborative nature of the proposed project, and identify potential partners: *(identify institutions, organizations, companies, and or consortia)*

This project is a direct outcome of the workshop described above which has already established a group of experts. The following institutions have already committed to working on this issue:

Academia: Stockholm University, University of Amsterdam

Government: ECCC, USEPA , RIVM, ECHA, OECD

Industry: RIFM, ExxonMobil, Givaudan, BASF, Shell, CONCAWE, ECETOC