2017 HESI Emerging Issues Proposal:

Development and Application of a Generic Tool for Performing Ecological Risk Assessments of Multiple Stressors

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Is this proposal submitted on behalf of more than one person / institution? If yes, identify co-submitters below.

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Proposal title: Development and Application of a Generic Tool for Performing Ecological Risk Assessments of Multiple Stressors

Key words: chemical mixtures, effluents, produced waters, species sensitivity distributions, mode of action, concentration addition, independent action, direct toxicity assessment, potentially affection fraction, risk assessment

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

Bonnefoi et al (2010) describes HESI's challenges for the next decade (2010–2020) include specific research and advances on "emerging contaminants", "multiple chemical", preservation of "environmental quality", development of "regulatory frameworks" and "computational tools". This proposal cross-cuts across all of these topics.

Chemicals management programs primary focus on assessing the risks of individual substances to determine if existing controls are adequate or if additional mitigation measures are required. However, an increasing regulatory and stakeholder concern is the potential cumulative effects of multiple chemical and non-chemical stressors, which individually may pose acceptable risk but collectively cause environmental harm. This concern is particularly relevant for freshwater and marine environments that receive long term, continuous wastewater discharges that may contain a wide range of potential chemical pollutants (inorganics, metals, organics) (ECETOC, 2011).

A practical approach for managing risks of effluent and produced water discharges is the use of whole effluent toxicity (WET) or direct toxicity analysis (DTA). These toxicity tests can be based on either acute or chronic in-vivo test endpoints and involve exposure of aquatic organisms to a serial dilution of the wastewater sample to assess the toxic potency. If multiple tests are performed a species sensitivity distribution (SSD) can be defined which defines the mean and variance of the observed toxicological response across different test species. Given a quantitative description of the SSD and an estimate of receiving water dilution the potentially affected fraction (PAF) of species affected via either acute or chronic exposure in the receiving environment can be estimated (Traas et al. 2002). As the magnitude of PAF increases the likelihood that site-specific risks will be observed in the field increases. An advantage of this approach is that interactive effects of the various measured and unmeasured stressors is directly assessed. Several disadvantages include increased animal use, potential confounding factors associated with lab testing of collected wastewaters (e.g. culture or collection of test animals, acceptable control performance) and costs relative to chemical analysis of wastewater contaminants.

A complimentary approach to DTA is application of toxicity models that predict effects of chemical mixtures using a detailed analysis of the expected wastewater contaminants (e.g. generic exposure profiles). For example, in the case of produced water discharges associated with oil and gas extraction, common chemical stressors that pose an aquatic hazard include ammonia, hydrogen sulfide, hydrogen cyanide, selected trace metals, speciated and unspeciated hydrocarbons that comprise the lower boiling range of total petroleum hydrocarbons and alkylphenols. Similar generic exposure profiles can be defined for other wastewaters relevant to different sectors based on process knowledge, emission inventories and historical wastewater quality characterization data. Given a list of potential contaminants, each substance can then be assigned into different assumed modes of action (MoAs) based on available toxicological knowledge (Kienzler, A. et al 2014). Empirical toxicity data (EPA ECOTOX database or EU REACh registration dossiers) or quantitative models (Kipka & DiToro, 2009; Chen et al. 2015) to predict aquatic hazards across species can then be used to define the SSDs for each contaminant included in the exposure profile.

Mixture toxicity associated with a wastewater profile can be assessed by assuming that substances with a common MoA act additively and that substances with different or unknown MoAs act independently. Analogous to the calculation of PAF using the DTA discuss above, this framework can be used to calculate a multiple stressor potentially affected fraction (msPAF) (De Zwart and Posthuma 2005). This approach is gaining increase use for assessing the ecological risks of chemical mixtures and is been the subject of several lab and field validation efforts (Olmstead et al. 2005; Posthuma et al. 2006, 2012). This framework provides the potential to link DTA and contaminant characterization approaches in order to identify known contaminants that dictate risks or unknown contaminants that warrant further analytical characterization. Results can also inform more focused wastewater monitoring requirements by targeting risk-driving contaminants and reducing or eliminating direct animal testing. A further advantage of the msPAF methodology is potential extension to include other media (e.g. soil, sediments) as well as non-chemical stressors (heat, solids, radioactivity, pathogens).

A practical limitation of implementing the DTA-based PAF and chemical-based msPAF approaches for ecological risk evaluation and subsequent management and monitoring of wastewater quality is the lack of a consistent, generic tool that can be customized by users from different sectors to provide these calculations. The objectives of this project are re two-fold. First, develop and publish a generic, user-friendly tool that can be used to support PAF and msPAF analyses. Second, apply and evaluate the insights that can be gained from this tool using two case studies that illustrate different sector-specific wastewater exposure profiles.

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.

A three-phased research program is proposed.

In Phase I, the key elements of the generic tool will be discussed and agreed via a targeted workshop that will be held at SETAC Europe in May 2017 or North America in November 2017 (depending on timing of the decision for successful proposals). This workshop will include a small steering group (10-12) of invited participants representing practitioners engaged in development and application of the methods discussed above and interested HESI stakeholders. The deliverable from this workshop will be a research proposal that can then be solicited for competitive bid for developing this tool.

In Phase II (year 2), the steering group will evaluate bidder responses, select the best qualified contractor for developing the tool, provide project oversight and initial beta testing of the tool and provide comment on user manual and peer-reviewed publication documenting tool.

In Phase III (year 3), HESI members will be provided with the tool for piloting using sector specific data sets. Two case studies will be selected for publication to illustrate practical use and insights gained with support from the contractor selected in Phase II.

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

The availability of a consistent, state of science tool would enable a systematic response across different sectors to address increasing expectations by regulators and stakeholders regarding cumulative risks posed by wastewater discharges. This work also provides a specific opportunity to reduce potential animal use in toxicity testing as well as environmental monitoring costs.

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

<u>List of key collaborators and rationale for involvement are summarized below</u>:

RIVM: Dutch regulators within this organization have been key developers of the msPAF methodology

Proctor & Gamble: This organization has had active collaboration with RIVM in for more than a decade in applying mixture toxicity methods for assessing ecological risks of down-the-drain consumer products

ExxonMobil and Shell: These organizations have been active in advancing mixture toxicity models for complex petroleum substances and have expressed interested in further extending this experience to other refinery effluents and produced waters. Mathijs Smit and Graham Whale have expressed specific interest in this project.

USEPA: This organization has served a central role in DTA and have supported the development of databases and *new mechanistic hazard models that can be used to derive substance specific SSDs.*

The European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM): This organization has stated that msPAF approaches can provide better, mechanistically based prediction of mixture effects but more guidance is needed for practical application.

Academia: Allen Burton (Univ. Michigan) and Hans Sanderson (Aarhus Univ., Denmark) are two key leaders in North America and Europe that have active experience developing and communicating practical tools to industry, regulators and the public.

We also propose soliciting collaboration with a HESI member representing the agrochemicals and/or pharmaceuticals sector.

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