ORIGINAL ARTICLE

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Pellston mixtures

L. Postuma et al.

Land use and mixture exposure scenarios for risk assessment

SIMPLIFYING ENVIRONMENTAL MIXTURES—AN AQUATIC EXPOSURE-BASED APPROACH VIA LAND USE SCENARIOS

LEO POSTHUMA,[a,b,]* COLIN BROWN,[c] DICK DE ZWART,[d] JERRY DIAMOND,[e] SCOTT D. DYER,[f] MICK HAMER,[g] CHRISTOPHER M. HOLMES,[h] STUART MARSHALL,[i,1] and G. ALLEN BURTON, JR.[j]

[a]National Institute for Public Health and the Environment (RIVM), Centre for Sustainability, Environment and Health, Bilthoven, The Netherlands

[b]Radboud University, Department of Environmental Science, Institute for Wetland and Water Research, Faculty of Science, Radboud University, Nijmegen, The Netherlands

[c]University of York, Environment Department, Heslington, York, United Kingdom

[d]Mermayde, Groet, the Netherlands

[e]Tetra Tech, Owings Mills, Maryland, USA

[f]The Procter and Gamble Company, Cincinnati, Ohio, USA

[g]Syngenta, Jealott's Hill, Bracknell, United Kingdom

[h]Waterborne Environmental, Leesburg, Virginia, USA

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[i]Unilever, Safety and Environmental Assurance Centre, Unilever, Sharnbrook, Bedford, United Kingdom

[j]University of Michigan, Ann Arbor, USA

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* Address correspondence to Leo.Posthuma@rivm.nl

[1]Retired.

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INTRODUCTION

Exposure to chemical mixtures is a fact of life. Therefore, the expectation would be that mixture risk assessments are common, but this is not the case. This may relate partly to the immense variability of mixture exposures that may occur, which would place an additional burden on the already immense task of regulating vast numbers of individual chemicals (e.g., **<ZAQ;1>**Hartung and Rovida 2009; Hendriks 2013). It may also relate to difficulties in bridging the science–practice interface: are scientifically sound methods ready to be applied, and what formats do they take?

Some technical guidance documents have handled mixtures by assuming that potential mixture effects are sufficiently addressed via the application factors that are already in use to derive regulatory protective concentration criteria from available ecotoxicity data. Given frequent concerns voiced on mixture exposures, various other approaches to mixture risk assessment may be needed in addition to application factor approaches, ranging from prospective methods that help to evaluate whether environmental and human health protection is sufficient under conditions of realistic mixture exposures, to retrospective methods that characterize the risk of polluted environmental compartments using measured data.

PELLSTON WORKSHOP ON MIXTURES

Given that mixture exposures (e.g., US Environmental Protection Agency 2009), risks (e.g., Malaj et al. 2014), and impacts (e.g., Posthuma et al. 2016) are common, and given that consensus approaches are available for practical risk assessments (e.g., Kortenkamp et al. 2009), the challenge is to operationalize methods that can handle the immense diversity of mixture exposures. This challenge was taken up by the Society for Environmental Toxicology and Chemistry (SETAC) Pellston workshop® "Simplifying environmental mixtures—an aquatic exposure-based approach via exposure scenarios," which was held in March 2015 in Valencia, Spain. The basis of the workshop was the idea that although mixtures can be immensely complex in their nature when considering separate chemicals and their concentrations, it may be expected that specific land uses could imply**<ZAQ;2>** specific, recognizable signatures of chemical emissions. Would algae, daphnids, fish, or whole species assemblages "recognize" that they were exposed to a mixture that can be seen as a multiconstituent compound from city runoff, or from agricultural land use upstream, or from wastewater treatment plant (WWTP) emissions? It was hypothesized that it is likely that land use is associated with distinct emission profiles, and that such profiles could be helpful in operational prospective and retrospective mixture assessments.

The SETAC Pellston workshop addressed the need to improve on mixture risk assessments by looking at land use related exposure scenarios. The aims of the workshop were 1) to investigate whether a simplified scenario-based approach could be used to help determine whether mixtures of chemicals posed a risk greater than that identified using single-chemical based approaches, and if so, 2) what might be the magnitude and temporal aspects of the risks associated with mixture exposures, thereby 3) determining whether the application of the approach provides insights in mixtures of greatest concern, and the compounds dominating those mixtures (prioritization).

APPROACHES TO MIXTURE SCENARIOS AND RISKS

The workshop defined 4 scenarios with typical chemical emission signatures, namely: 2 agricultural land use scenarios (1 in the United States and 1 in Europe), an urban storm water runoff scenario, and a scenario looking at emissions of household chemicals via WWTPs. The scenarios were specified and the chemicals that may be emitted from them were investigated via literature research, survey databases, and querying expert users. Existing and custom emission models were used.

Efforts focused on characterizing the land-use based emissions and the chemical identities typically emitted from these land uses. Subsequently, exposure scenarios were defined and investigated. Resulting mixture exposures were evaluated in a tiered fashion, most often via risk characterization ratios (defined as the ratio of exposure concentration and an ecotoxicity endpoint) aggregated over compounds in the mixture by assuming concentration additivity as the default model.

WORKSHOP RESULTS

The workshop discussions and analyses resulted in 4 research articles, published in this issue of *Environmental Toxicology and Chemistry*: 1) Holmes et al. 2018, "Prospective aquatic risk assessment for chemical mixtures in agricultural landscapes;" 2) Diamond et al. 2018, "Use of prospective and retrospective risk assessment methods that simplify chemical mixtures associated with treated domestic wastewater discharges;" 3) De Zwart et al. 2018, "Aquatic exposures of chemical mixtures in urban environments: Approaches to impact assessment;" and

4) Posthuma et al. 2018, “Prospective mixture risk assessment and management prioritizations for river catchments with diverse land uses.”

Holmes et al., Diamond et al., and De Zwart et al. describe the specifications of 3 specific land use and exposure scenarios, and the associated risks of the associated chemical mixtures, including the analysis of the relative contributions of chemicals to the mixture risks. Holmes et al. and Posthuma et al. describe full land use–based emission—exposure—mixture risk model**<ZAQ;3>** approaches, in which the emissions were combined with a suite of realistic data on rainfall events, storm water overflows, plant protection, veterinary product applications, and hydrology. Following this mimicking of realistic land use exposure scenarios, these studies resulted in a systematic, tiered set of mixture risk assessments. Mixture risk assessments were thereby increasingly specific regarding the exposure variation over time (related, e.g., to weather and applications) and the taxonomic groups potentially affected.

MAIN FINDINGS

Based on data reviews and (in part) modeling, the 4 studies illustrated that specific land uses likely result in aquatic environments being exposed to typical sets of chemicals. The exposures were further characterized by typical time-related patterns (e.g., relatively continuous exposures resulting from the emissions of household chemicals, and more variable over time for city runoff and agriculture). The studies further generated evidence to support the need to prospectively consider mixtures in addition to single compounds, because (based on a concentration-additive risk assessment assumption) situations considered sufficiently protected with regard to single-chemical emissions appeared insufficiently protected in realistic mixture scenarios. Within the scenarios, there was evidence to suggest that the taxonomic groups most likely affected could be identified in higher tiers of the assessment. **<ZAQ;4>**There was also evidence to suggest that in many cases the occurrence of predicted mixture risks can be attributed to relatively few compounds. The latter has been observed more frequently based on measured environmental concentrations (e.g., Backhaus and Karlsson 2014; Vallotton and Price 2016). One of the common characteristics of mixture risk assessments is a difference in the availability of ecotoxicity data for the compounds involved in causing the potential risk. The studies that resulted from the SETAC Pellston workshop “Simplifying environmental mixtures—an aquatic exposure-based approach via exposure scenarios,” illustrate that this may result in an interpretation pitfall, when an apparently large contribution of a compound to the mixture risk is not necessarily associated with greatest toxicity, but rather with greatest uncertainty (least data). Overall, the methods that were explored support the prioritization of mixtures for further investigation or management.

POTENTIAL IMPLICATIONS

The results imply that risk assessment and associated risk management strategies may be developed, potentially by the solution-focused approach to risk assessment (e.g., National Research Council 2009; Munthe et al. 2017), by focusing on a few multiconstituent compounds—the typical mixtures found downstream of a land use—rather than solely on all individual compounds. The set of articles suggests that emissions from true catchments and land uses can be addressed through science-based approaches that consider exposure scenarios for a wide range of ecosystems and land use types.

The proposed approach for evaluating chemical mixture risks has a wide range of potential applications. **<ZAQ;5>**This can be supported by the development of a set of typical road maps— scenarios with typical emissions, exposure, and risk signatures. These scenarios can serve both prospective and retrospective risk assessments, and could also support the development of cost-effective management actions that may be as typical to the land uses as the typical chemical signatures. Opportunities to reduce the emissions caused by city runoff are different from those to reduce emissions from household chemicals or agricultural chemicals (Munthe et al. 2017; Van Wezel et al. 2017), and this has recently been recognized as basis, for example, for storm water management and urban planning (Sharley et al. 2017).

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Disclaimer—The opinions expressed in the present study are those of the authors and not their respective employers.

Data availability—Correspondence may be addressed to Leo.Posthuma@rivm.nl.

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Figure Captions

<<ENOTE>>AQ1: Please clarify. What are these citations examples of?

<<ENOTE>>AQ2: Verify word choice – “involve”? Or, “…it may be possible to infer specific, recognizable signatures of chemical emissions from specific land uses.” Instead of “imply”

<<ENOTE>>AQ3: Confusing dashes. Reword to clarify, or is that the appropriate phrasing for that model?

<<ENOTE>>AQ4: Please confirm rewording. “There was also evidence…few compounds”

<<ENOTE>>AQ5: Please clarify what the subject is. The proposed approach or the potential applications?

<<ENOTE>>AQ6: Please spell out CEFIC-LRI, CONCAWE, ERASM, and ECETOC. Please consult with companion paper authors to ensure that these are spelled out consistently throughout.