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**Environmental Toxicology
& Chemistry**

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

Journal:	<i>Environmental Toxicology and Chemistry</i>
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Mandatory Keywords:	mixtures, ecological risk assessment, environmental chemistry
Additional Keywords (Optional):	land use, scenario
Abstract:	Exposure to chemical mixtures is a fact of life. Mixture risk assessments should therefore be common, but that is not the case. As mixture exposures, risks and impacts are common, and as consensus approaches are available for practical risk assessments, the current challenge is to operationalize methods that can handle the immense diversity of mixture exposures. This challenge was taken up by the SETAC Pellston® workshop "Simplifying environmental mixtures - an aquatic exposure-based approach via exposure scenarios" which was held in March 2015 in Valencia, Spain. The outcomes of the workshop are summarized in a series of four consecutive papers. Those consider exposures and risks of mixtures of chemicals related to various land use example scenarios. Based on the overall set of results, it is concluded that mixture risk assessments via land use exposure scenarios provide useful and necessary insights into the potential effects of mixtures in the environment.

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11 **2 SIMPLIFYING ENVIRONMENTAL MIXTURES –**
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This list might apply if authors are needed at all!!

For now the list is alphabetic, constructed from the name list of the workshop organizers / paper-series conference call regular attendants.

The list can be adapted for sure.

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26 **Running Head:**
27 Land use and mixture exposure scenarios for risk assessment

28 **Word count: 1324 words.**

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10 30 **INTRODUCTION**

11 31 Exposure to chemical mixtures is a fact of life. Therefore the expectation would be that mixture
12 32 risk assessments are common, but that is not the case. This may relate partly to the immense
13 33 variability of mixture exposures that may occur, which would place an additional burden on the
14 34 already immense task of regulating vast numbers of individual chemicals (e.g., Hartung and
15 35 Rovida (2009), Hendriks (2013)). It may also relate to difficulties in bridging the science-
16 36 practice interface: are scientifically sound methods ready to be applied, and what formats do they
17 37 take?

18 38 So far, some technical guidance documents have handled mixtures by assuming that potential
19 39 mixture effects are sufficiently addressed via the application factors that are already in use to
20 40 derive regulatory protective concentration criteria from available ecotoxicity data. Given
21 41 frequent concerns voiced on mixture exposures, various other approaches to mixture risk
22 42 assessment may be needed in addition to application factor approach, ranging from prospective
23 43 methods that help to evaluate whether environmental and human health protection is sufficient
24 44 under conditions of realistic mixture exposures, to retrospective methods that characterize the
25 45 risk of polluted environmental compartments using measured data.

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28 47 **PELLSTON WORKSHOP ON MIXTURES**

29 48 As mixture exposures (e.g., USEPA (2009)), risks (e.g., Malaj, von der Ohe et al. (2014)) and
30 49 impacts (e.g., Posthuma, Dyer et al. (2016)) are common, and as consensus approaches are
31 50 available for practical risk assessments (e.g., Kortenkamp, Backhaus et al. (2009)), the challenge
32 51 is to operationalize methods that can handle the immense diversity of mixture exposures. This

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challenge was taken up by the 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 whilst 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 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 ‘multi-constituent compound’ from city run-off, or from agricultural land use upstream, or from wastewater treatment plant 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 to mixture exposures, so as:

(3) to determine whether the application of the approach provides insights in mixtures of greatest concern, and the compounds dominating those mixtures (prioritization).

71

46 72 APPROACHES TO MIXTURE SCENARIOS AND RISKS

73 The workshop defined various scenarios with typical chemical emission ‘signatures’, namely:
74 two agricultural land-use scenarios (one in the U.S and one in Europe), an urban storm water

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75 run-off scenario, and a scenario looking at emissions of household chemicals via wastewater
76 treatment plants. The scenarios were specified and the chemicals that may be emitted from them
77 were investigated via literature research, survey databases, and querying expert users. Existing
78 and custom emission models were used.

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

85
86 **WORKSHOP RESULTS**
87 The workshop discussions and analyses resulted in four research papers, published in this issue
88 of *Environmental Toxicology and Chemistry*:

- 89 (1) Holmes, Brown et al. (2017 (in press)). Prospective aquatic risk assessment for chemical
90 mixtures in agricultural landscapes;
- 91 (2) Diamond, Altenburger et al. (In press (2017)). Use of prospective and retrospective risk
92 assessment methods that simplify chemical mixtures associated with treated domestic
93 wastewater discharges;
- 94 (3) De Zwart, Adams et al. (In press 2017). Aquatic exposures of chemical mixtures in urban
95 environments: approaches to impact assessment;
- 96 (4) Posthuma, Brown et al. (2017 (early online)). Prospective mixture risk assessment and
97 management prioritizations for river catchments with diverse land uses.

98 The papers of Holmes et al., Diamond et al., and De Zwart et al. describe the specifications of
99 three specific land use- and exposure scenarios, and the associated risks of the associated
100 chemical mixtures, including the analysis of the relative contributions of chemicals to the
101 mixture risks. The papers of Holmes et al. and Posthuma et al. describe full land-use based
102 emission – exposure – mixture risk model approaches, in which the emissions were combined
103 with a suite of realistic data, e.g. on rainfall events, stormwater overflows, plant protection and
104 veterinary product applications and hydrology. Following this mimicking of realistic land use
105 exposure scenarios, these studies resulted in a systematic, tiered set of mixture risk assessments.
106 Mixture risk assessments were thereby increasingly specific regarding the exposure variation
107 over time (related to e.g. weather and applications) and the taxonomic groups potentially
108 affected.

110 **MAIN FINDINGS**

111 Based on data reviews and (in part) modelling, the four studies illustrated that specific land uses
112 likely result in aquatic environments being exposed to typical sets of chemicals. The exposures
113 were further characterized by typical time-related patterns (e.g., relatively continuous exposures
114 resulting from the emissions of household chemicals, and more variable over time for city run off
115 and agriculture). The studies further generated evidence to support the need to prospectively
116 considering mixtures in addition to single compounds, as (based on a concentration-additive risk
117 assessment assumption) situations considered sufficiently protected regarding single-chemical
118 emissions appeared insufficiently protected in realistic mixture scenarios. Within the scenarios,
119 there was evidence to suggest that the taxonomic groups likely most affected could be identified
120 in higher tiers of the assessment and there was also evidence to suggest that in many cases the

121 occurrence of mixture risks can be attributed to relatively few compounds contributing most to
122 the predicted risk. The latter has been observed more frequently based on measured
123 environmental concentrations (e.g., Backhaus and Karlsson (2014) Vallotton and Price (2016)).
124 One of the common characteristics of mixture risk assessments is a difference in the availability
125 of ecotoxicity data for the compounds involved in causing the potential risk. The studies
126 illustrate that this may result in an interpretation pitfall, when an apparently large contribution of
127 a compound to the mixture risk is not necessarily associated with greatest toxicity, but rather
128 with greatest uncertainty (least data). Overall, the methods that were explored support the
129 prioritization of mixtures for further investigation or management.

130
131 **POTENTIAL IMPLICATIONS**
132 The result imply that risk assessment and associated risk management strategies may be
133 developed, potentially by the solution-focused approach to risk assessment (e.g., U.S. NAS
134 (2009), Munthe, Brorström-Lundén et al. (2017)), by focusing on a few 'multi-constituent
135 compounds' – the typical mixtures found downstream of a land use – rather than solely on all
136 individual compounds. The set of papers suggests that emissions from true catchments and land
137 uses can be addressed through science-based approaches that consider exposure scenarios for a
138 wide-range of ecosystems and land-use types.

139 The proposed approach for evaluating chemical mixture risks has a wide range of potential
140 applications. This can be supported by the development of a set of typical "road maps", being
141 scenarios with typical emissions, exposure and risk signatures. These scenarios can serve both
142 prospective and retrospective risk assessments, and could also support the development of (cost-
143)effective management actions that may be as typical to the land uses as the typical chemical

144 signatures. Opportunities to reduce the emissions caused by city run-off are different from those
145 to reduce emissions from household chemicals or agricultural chemicals (Munthe, Brorström-
146 Lundén et al. 2017, Van Wezel, Ter Laak et al. 2017), and this has recently been recognized as
147 basis for e.g. stormwater management and urban planning (Sharley, Sharp et al. 2017).

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30 155 **Disclaimer** – The opinions expressed in the present study are those of the authors and not
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32 156 their respective employers.

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