

Original Article

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Pellston Mixtures

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Blending mixture exposure scenarios for risk assessment

PROSPECTIVE MIXTURE RISK ASSESSMENT AND MANAGEMENT

PRIORITIZATIONS FOR RIVER CATCHMENTS WITH DIVERSE LAND USES¹

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Abstract

Ecological risk assessment increasingly focuses on risks from chemical mixtures and multiple stressors because ecosystems are commonly exposed to a plethora of contaminants and nonchemical stressors. To simplify the task of assessing potential mixture effects, we explored 3 land use–related chemical emission scenarios. We applied a tiered methodology to judge the implications of the emissions of chemicals from agricultural practices, domestic discharges, and urban runoff in a quantitative model. The results showed land use–dependent mixture exposures, clearly discriminating downstream effects of land uses, with unique chemical “signatures” regarding composition, concentration, and temporal patterns. Associated risks were characterized in relation to the land-use scenarios. Comparisons to measured environmental concentrations and predicted impacts showed relatively good similarity. The results suggest that the land uses imply exceedances of regulatory protective environmental quality standards, varying over time in relation to rain events and associated flow and dilution variation. Higher-tier analyses using ecotoxicological effect criteria confirmed that species assemblages may be affected by exposures exceeding no-effect levels and that mixture exposure could be associated with predicted species loss under certain situations. The model outcomes can inform various types of prioritization to support risk management, including a ranking across land uses as a whole, a ranking on characteristics of exposure times and frequencies, and various rankings of the relative role of individual chemicals. Though all results are based on *in silico* assessments, the prospective land use–based approach applied in the present study yields useful insights for simplifying and assessing potential ecological risks of chemical mixtures and can therefore be useful for catchment-management decisions.

Keywords: Chemical mixture, Aquatic risk assessment, Watershed management, Catchment assessment, Exposure scenario, Ecological risk assessment

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INTRODUCTION

The present study is an output of a Society of Environmental Toxicology and Chemistry (SETAC) Pellston workshop®, “Simplifying Environmental Mixtures —An Aquatic Exposure–Based Approach Via Exposure Scenarios,” which was held in March 2015 with the aim of looking at 1) whether a simplified scenario-based approach could be used to help determine if mixtures of chemicals posed a risk greater than that identified using single chemical–based approaches and 2), if so, what might be the magnitude and temporal aspects of the exceedances 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). The aims of the present study were to combine the land-use scenarios of the associated manuscripts of the Pellston workshop, references Holmes et al. (2018), Diamond et al. (2018), and De Zwart et al. (2018), to investigate these questions for catchments with different combinations of land use.

The goal of various environmental policies in human-dominated ecosystems is to achieve a nontoxic environment and sound biological integrity (European Commission). This status has not been reached in many freshwater and marine systems, based on evidence on the occurrence

of a wide array of chemicals in surface waters (Bradley et al. 2017) and organisms' tissues (US Environmental Protection Agency 2009), with associated evidence for multiple contaminant risks (Malaj et al. 2014), impacts in bioassays (Conley et al. 2017), and reduced species biodiversity and abundance in various human-dominated systems (Schäfer et al. 2016; Posthuma et al. 2016). Achieving negligible exposures and nontoxic conditions is challenging given the multitude of chemicals associated with human sources such as agricultural practices, treated wastewater, and urban runoff. Currently produced chemicals may cause direct species loss but also effects such as fish intersex and possibly other unknown effects (Kolpin et al. 2002), and new chemicals are continuously produced and emitted (Gessner and Tlili 2016). Regulatory approaches regarding chemicals presently focus, however, on a relatively small number of chemicals for which there are established environmental quality standards (EQS). Less is known about how to assess and reduce the risks and effects of ambient mixtures.

The assessment and management of ecological risk for a highly complex matrix of combinations of chemicals, sites, species, and ecosystems can proceed via various approaches. The traditional approach is based on risk assessment of individual chemicals, using generic protective EQS. Those are benchmark concentrations, such as the predicted no-effect concentration (PNEC). A predicted or measured environmental concentration (PEC or MEC) below such a threshold is interpreted as protective of ecosystem structure and function, that is, the risk quotient ($RQ = PEC/\text{benchmark concentration}$ or $RQ = MEC/\text{benchmark concentration}$) is <1 . The origin of these methods dates back to the 1970s and 1980s (Stephan et al. 1985; Van Straalen and Denneman 1989). Since then tailored methods have been defined to serve specific policy goals, such as generic water quality policies and policies to determine the environmental hazards of plant protection products (PPPs) for aquatic edge-of-field exposures (Geiser 2015). Recently, chemical mixture assessment approaches have been recommended for practical application (Kortenkamp et al. 2009). Many of these mixture approaches evaluate mixture risks by a default approach via aggregation of the individual RQs for each chemical in the mixture, such as the hazard index ($HI = \sum RQ = \sum [PEC/\text{benchmark concentration}]$), although the expected mixture effects are also quantified via mixture toxic pressures for species assemblages, expressed as multisubstance potentially affected fraction (msPAF) of species (De Zwart and Posthuma 2005). In addition, various methods are available to retrospectively evaluate the ecological risks and impacts of mixtures on the landscape scale (Posthuma et al. 2016). The latter approaches offer an a posteriori quantitative risk or impact ranking of sites and stressors of concern (including chemical mixtures).

In the present study we describe a prospective analysis of land use–related emissions, exposures, and risks of chemical mixtures. This concerns both the resulting chemical signatures (are there land use–specific mixture compositions [Holmes et al. 2018; Diamond et al. 2018; De Zwart et al. 2018]?) as well as the resulting chemical footprints (is there a net risk exported from a catchment to a downstream water body [Zijp et al. 2014; Bjørn et al. 2014]?). Prospective, catchment-scale prioritization of chemical mixture risks can assist decision-making regarding risk-mitigation strategies (Ginebreda et al. 2013; Coppens et al. 2015; Sobek et al. 2016; Brack et al. 2017). The present study expands on and integrates 3 detailed analyses of land use–related scenarios, investigating the specific chemical signatures of an agriculture scenario (emissions from agricultural land dictated by rainfall, soils, and PPP use [Holmes et al. 2018]), a treated domestic wastewater scenario (daily use of household chemicals [Diamond et al. 2018]), and an urban runoff scenario (rainfall-mediated emissions from city surface areas [De Zwart et al. 2018]).

The goal of the present study was to develop and test the utility of combining the concepts of continuous exposure of treated domestic wastewater discharge with temporally variable chemical exposure scenarios associated with urban and agricultural land uses for the purpose of supporting comprehensive mixture risk assessments and environmental management. To achieve this, the following objectives were addressed: 1) propose and evaluate an approach for deriving a likely chemical signature in a receiving river catchment to help explain field observations (concentrations and/or impacts) and provide a background against which the toxicity of a new product or a new usage could be assessed, 2) produce an approach balancing pragmatism and simplicity with adequate detail for a scientifically credible outcome, 3) recognize the complexity of assessing both the exposure and effects of mixtures and derive generalizations that provide evidence for a reality check of ecological risk assessment, and 4) identify uncertainties and gaps in knowledge requiring further research to refine the prospective assessment of chemical mixtures.

COMBINED SCENARIOS

Overall approach

We integrated risk-assessment approaches for 3 typical human-based emission scenarios (agriculture, domestic, urban runoff) and focused on identifying the potential for mixture effects in receiving waters. The scenarios were selected because they commonly occur in human-dominated systems and differ vastly in their chemical emission characteristics. The scenarios were further developed and substantiated as land-use scenarios, whereby domestic and urban runoff are combined as the land use CITY. Further, the land use nature was added for demonstrating the influence of water inputs within the catchment where chemical emissions are negligible. The scenarios were combined in a catchment-assessment model, with the option to define land uses for between 1 and 10 subcatchments. Their integration placed the different single land-use categories into a landscape-level perspective. This allowed for cross-comparisons and integrated exposure and risk analyses, to evaluate the utility and limitations of land-use scenarios for environmental assessment and potential management of chemical mixtures.

Modeling land uses, geography, and hydrology

The scenarios agriculture, CITY (domestic+urban runoff), and nature were spatially combined in hypothetical but realistic spatial arrangements to represent either a single-land use scenario in a subcatchment or a catchment with multiple land uses and river confluences. A spreadsheet model represented the various catchment layouts. The model included hydrology, aquatic emissions, concentrations, and mixture assessment outcomes for (in its most complex format) a catchment of 100 km² with 10 subcatchments of 10 km² each, linked within a river network (Figure 1). A subcatchment was defined to have only one land use. A catchment can have any combination and number of subcatchments (in our case, up to 10) and assigned land uses. The land uses shown in Figure 1 define the layout of the modeled MIXED land-use scenario, which is just one of many possible catchment layouts.

The characteristics of the separate emission scenarios (agriculture, domestic, urban runoff, and nature) were developed based on literature reviews and by combining hydrological and ecotoxicological modeling techniques with regulatory judgment criteria (Table 1). Each scenario layout was modeled for 20 yr, with daily quantifications of PECs for the each of the

studied chemicals. Details are in the Supplemental Data (section 1) and the scenario reviews (Holmes et al. 2018; Diamond et al. 2018; De Zwart et al. 2018).

Modeling concentrations

Emissions of chemicals from agriculture, domestic, and urban runoff were derived from individual land-use studies (details in those reviews and the Supplemental Data). The agriculture scenario incorporated time dependency of emissions related to PPP use on row crops. A 20-yr time period was modeled on a daily basis by using actual pesticide usage application data for a large arable farm in eastern England (see Holmes et al. 2018) and actual rain events from the FOCUS R1 scenario meteorological data set (used in European Union regulatory modeling for PPPs), which is directly applicable to United Kingdom agricultural conditions. The selected agriculture scenario used a winter wheat exposure scenario, with 13 active ingredients applied on known dates and rates. Accordingly, the scenarios for the other emissions (domestic, urban runoff) were reformulated to enable modeling for the same 20-yr period and combined into the spreadsheet model. Emission data and hydrological data were combined to estimate concentrations for each of the studied chemicals emitted from each of the land uses.

The spreadsheet model allowed the prediction of concentrations from agriculture, domestic, and urban runoff emissions separately as well as their combinations based on the subcatchment configuration (Figure 1). The model yields 24-h PECs for subcatchment outlets. Large numbers of PECs were calculated using this approach. For example, for agriculture the number of PECs equals 94 198 (7246 d, 13 chemicals) and for MIXED, 268 102 (7246 d, 37 compounds).

Risk-assessment methodologies and prioritizations

The risk patterns associated with the PECs were explored using 3 approaches: HIs, maximum cumulative ratios (MCRs; Vallotton and Price 2016), and mixture toxic pressures (multisubstance potentially affected fraction of species, [msPAF; De Zwart and Posthuma 2005]). Details are in Supplemental Data (section 2).

First, the risks posed by a mixture were determined using individual chemical hazard quotients (HQs) and the net HI, in which $HQ_{ij} = PEC_i/BM_{ij}$ (with i = substance, j = selected effect endpoint, with j defined as regulatory EQS, chronic no-observed-effect concentration [NOEC], or acute median effect concentration [EC50], see below), and $HI_j = \sum HQ_{ij}$. The HI is the sum of the individual values of compound-related HQs, implying the use of concentration additivity as a default mixture model.

Second, the MCR is the maximum cumulative ratio posed by a combined exposure to multiple chemicals under the assumption of concentration addition divided by the risk of the most toxic compound of the sample. The MCR of a sample expresses whether the net predicted toxicity is driven by multiple components which make a significant contribution to the net mixture toxicity. The MCR-value of a sample was calculated as the ratio of the sample's HI and the highest value of the sample's set of values: $MCR = HI/\max(HQ)$. The combination of HI and MCR was used to create subgroupings of the 7246 time samples per scenario in 4 groups: groups I, II, IIIA, and IIIB (Table 2).

The HI-MCR method was applied using different benchmark definitions to derive the HI, representing different tiers and meanings. For tier 1, HIs were defined by generic, protective regulatory criteria (the annual average EQS [AA-EQS] of the European Water Framework Directive). For tier 2, HIs were defined via the 5th percentile of the species sensitivity

distribution (SSD) of chronic NOECs and the 50th percentile of the SSD of EC50s. For tier 3, the MCR was plotted against the mixture toxic pressure (msPAF), derived from the SSD models (SSD_{NOEC} and SSD_{EC50}, respectively). In tier 1, HI >1 indicates regulatory concern, whereby it remains uncertain whether direct ecotoxicological effects are likely, for example, because of underlying application factors. In tiers 2 and 3, HI >1 is interpreted as a signal for direct chronic or acute effects on species assemblages, while these HIs have no maximum. In tier 3, in addition, the predicted mixture impact is maximized to 100% of species affected at a chronic or an acute level, respectively. The MCR axis is interpreted as to the number of compounds contributing to the mixture risk.

The scenario results were also summarized as chemical footprints (Zijp et al. 2014). A chemical footprint expresses whether the net emissions in a landscape remain within a preset boundary on risks or effects, for example, the mixture exposure level at which 95% of the species is protected against exceedance of their no-effect level for the mixture (msPAF_{NOEC} <0.05). In the present study, the approach is modified to summarize the percentage of days the latter is exceeded at the outflow of a subcatchment based on the P95 of the msPAF_{NOEC} of all days of a scenario run.

RESULTS

Rainfall and flow

The natural rainfall varied over time and resulted in variation in flow. The vast numbers of input data on rain and output data generated on flow (7246 per scenario) are summarized in Supplemental Data (section 3). The outputs show that the variation in flow implied a strong influence on the dilution of emitted chemical loads and domestic discharge effluents. Summarized as the P99.9/P5 flow ratios, the high to low flow ratios were 55, 324, 128, and 94 for the scenarios CITY, agriculture, nature, and MIXED, respectively.

PECs

The temporal variability of PECs is illustrated in Figure 2. The chemical concentrations varied over time because of the sequential use of PPPs combined with rain events (agriculture) and rain events passing the runoff threshold of 10.3 mm rain (urban runoff). For domestic, though the per capita use of chemicals in this scenario was constant over time, the resulting PECs show spatiotemporal variation because of the effects of variations in hydrological conditions.

PECs and MECs

The PECs were compared to measured values (MECs obtained from available databases and literature (Figure 3; details in Supplemental Data, section 4). Averaged over the chemicals and as represented in the monitoring databases, the fractions of river water samples with measured concentrations higher than the limit of quantification (LOQ) were 1.4% for agriculture, 59.8% for domestic, and 14.1% for urban runoff chemicals. For many field samples (frequency for agriculture > urban runoff > domestic) the MECs were lower than the LOQ. The percentiles of the MEC distributions (Figure 3) therefore refer to the subset of samples with quantifiable concentrations and those of the PECs to the total set of 7246 predicted values for a compound.

For some chemicals, for example, pendimethalin in the agriculture scenario, the upper percentiles of European river water MEC distributions were very similar to the scenario-based PECs. For other chemicals, the highest MEC percentiles were greater (e.g., chlorothalonil) or lower (e.g., caffeine) than the higher PEC percentiles. Given the flow variation, the degree of similarity between detected MEC percentiles and PEC percentiles suggest that the land-use scenarios resulted in predicted exposures that may occur in European rivers.

Risk characterization step 1: PECs and exceedance of regulatory endpoints

Tier-1 results show that the regulatory benchmark concentrations were exceeded for various subcatchment outlet days and for various compounds ($HI > 1$, see Supplemental Data, Tables S7–S9). Looking at peak exposures (represented by P95-PEC), the peak PECs of, for example, pendimethalin exceeded the AA-EQS and the maximum annual concentration (MAC) as spelled out as maximum annual concentration? Abbreviation is not used elsewhere. concentration EQS of this compound 8 and 6 times, respectively. For the domestic scenario, the peak exposure of ethinylestradiol and galaxolide exceeded the AA-EQS 4 and 7.5 times, respectively. For the urban runoff scenario, the highest exceedance was found for deltamethrin, where the peak exposure was 1171 times the standard. Whether exceedances imply ecotoxic effects depends not only on the magnitude but also on the duration of exposure. This also varied. For example, for 7.3, 80, 91, and 5% of the days there was an exceedance of the AA-EQS of pendimethalin (agriculture), ethinyl estradiol (domestic), galaxolide (domestic), and deltamethrin (urban runoff), respectively. Exposures can thus be shorter or longer and frequent or incidental. These results suggest, from a regulatory perspective, that the river system at the outlet of a subcatchment or the whole catchment was not sufficiently protected, although high values may also result from high HQ values resulting from a high affected fraction related to high uncertainty on the benchmark (defining a low benchmark because of high data uncertainty).

Risk characterization step 2: Characterization of HIs of mixtures

The results of tier 1 were summarized as HI-MCR plots. The MIXED land use (Figure 1) resulted in the plotting of 7246 HI-MCA data points, which partly overlay each other (Figure 4). The figure suggest that the water at the outflow of the catchment frequently showed HI values (often $\gg 1$), which means that the RQs of individual compounds were (far) exceeded, while some of the HI points (with $HI > 10\,000$) are not shown. The latter values were found to be related to chemicals of mainly the urban runoff scenario, for days after peak rainfall (causing a runoff event) and for chemicals with low AA-EQS. The water system is judged to be insufficiently protected for 96% of the days, whereby the MCR remained below 6, with a high frequency of $MCR \cong 3$ and many $MCRs < 3$. The theoretical maximum MCR of the MIXED scenario is 37 (when the 37 compounds considered in this scenario are present at equitoxic concentrations, which is unlikely in nature). The relatively low MCRs suggest that a low number of compounds (always fewer than 7) induces $HI_{AA-EQS} > 1$. The high frequency of similar MCRs at a single level is attributable to a similar change of HI and the maximum HQ of a sample with dilution, because of which HI (X) can vary at nearly constant MCR (Y), whereas the typical HI-MCR pattern in the CITY scenario related to threshold effects (runoff > 10.3 mm rainfall). This threshold contributed to “forcing” the specific pattern of CITY-MCRs to 2 key MCR levels, related to runoff chemicals’ effect criteria.

The tier-2 analyses resulted in modified HI-MCR patterns, slightly shifted left for the criterion based on the 95th percentile protection level (Figure 5, upper graphs). Note that both

the HI and the MCA of a data point change when the standards underlying the HI change from AA-EQS to another effect criterion. A tier-2 evaluation based on EC50s resulted in a further shift of the data points to the left so that only few samples were found where PECs exceeded the EC50 of one or more compounds. Species loss was predicted for those samples, given an earlier observation that $msPAF_{EC50}$ relates to observed species loss in mixture-exposed aquatic systems (Posthuma and De Zwart 2012). Note that defining another tier-2 HI using, for example, an EC10 or EC25 as benchmark would result in intermediate shifts (Figure 5, between top and bottom), that is, between chronic exceedance of NOECs and the earliest onset of effects and species loss.

Exposure frequency and time are important in the process of causing ecotoxic effects. Whereas the data points of Figure 5, bottom, may indicate that peak exposures may induce species loss, the same is not true for the data points of Figure 5, top, because those points predict impacts under the condition that chronic exposure occurs. Investigations showed that the exposure times varied across the land uses. For the acute MIXED scenario, the percentage of days and the maximum number of consecutive days for which the mixture exposure $HI > 1$ are 0.1% and 4 d, respectively. The period of high exposure at the outflow of the MIXED scenario is commonly short, but there are a few instances of a few days of exceedance of the mixture EC50. For agriculture, the majority of days where $HI_{NOEC} > 1$ were for a single day. Only on 31 d (0.4%) was the exceedance 2 to 3 d, with no periods of 4 or more days with $HI_{NOEC} > 1$. In short, there was no chronic exposure. The exposure duration differed vastly for CITY, where the majority of days showed $HI_{NOEC} > 1$ (88% of days), and 98% of the exposure lasted at least a consecutive 4 d. The main CITY emission effects were reflected in the exposure durations of the MIXED scenario ($HI_{NOEC} > 1$ for 93% of days, and 86% of exposures lasting at least 4 consecutive days).

Risk characterization step 3: Mixture toxic pressures

The risk characterization in step 3 consisted of expressing the mixture risks as $msPAF_{NOEC}$ and plotting these outputs again vis à vis the MCAs. The results in Figure 6 suggest that the 95% protection level is exceeded on 8% of the days for agriculture and 100% of the days for CITY (as well as MIXED, not shown), while these chronic toxic pressure levels are associated most often with a few compounds in the mixtures (judged by the MCR values). The CITY and MIXED scenarios consisted of exposures of a chronic kind so that the land use would imply chronic effects for aquatic species assemblages. Acute effects though, quantified via $msPAF_{EC50}$, are more restricted. The maximum acute toxic pressure for agriculture would affect 8% of the species, whereby 1 out of 1000 species would be affected at the peak exposure days (P95 of $msPAF_{EC50} \cong 0.001$). For MIXED these values are 63% of the species at the day of the most toxic mixture outflow and 10% of the species at P95.

Prioritization

Various prioritization analyses can be made to underpin the choice of an abatement scenario aimed at water quality improvement. While in practice “ease of implementation” of abatement measures will be important too, we consider various rationales of risk-driven prioritization. Details are in Supplemental Data (section 4).

First, prioritization on the basis of land use showed the rank order of mixture risks of CITY (domestic+urban runoff) > agriculture for 3 HI definitions (Table 3). A tier-1 signal for regulatory concern was most frequent (exposure > AA-EQS), followed by the frequency of direct

sublethal ecotoxic effects (exposure > NOEC), with a low number of modeled samples with species loss of >50%. In the MIXED scenario, prioritizing the maximum HI's using the tier-2 approach resulted in the mixture risk rank order CITY (urban runoff+domestic) > MIXED >> agriculture (Table 3). The resulting chemical signatures (composition of mixtures and levels of exposure) clearly differ regarding land use.

Second, prioritizations for exposure periods also differ. The agriculture scenario was characterized by peak exposures (always <2 successive days with mixture HI >1), whereas CITY (urban runoff+domestic) and MIXED were characterized by chronically high HIs. Chemical signatures differed regarding exposure dynamics, and even the constant emission of domestic appeared highly dynamic related to hydrology. Further examples are in Supplemental Data, Table S10.

Third, the relative importance of chemicals was assessed. Many prioritizations can be made, for example, for tier 1, 2, or 3 evaluations in each scenario and then on a daily basis (determining the relative importance of each chemical on day = t , 7246 times per scenario) or for the numbers of days where the mixture HI >1. Outcomes are in Supplemental Data, Table S10. It appeared that risk prioritization outcomes depend heavily on the tier and inherent risk characterization method. For agriculture, chlorothalonil was, for example, sixth in rank when judged by the AA-EQS definition of HI but first when judged by chronic SSD_{NOEC}-HI. Again, prioritization needs to account for temporal aspects. Chemicals in domestic would have priority when considering the more chronic character of domestic exposures over urban runoff exposures, while the latter contribute more to the risk of mixtures when present after a runoff event. Comparison to the individual scenario studies demonstrated that the prioritizations shown in Supplemental Data, Table S10, are in line with the outcomes of those scenario studies. For agriculture in the present study, cypermethrin, pendimethalin, and chlorothalonil were found to be important regarding peak exposure levels, ranking first, second, and third, respectively, using AA-EQS to define HI. Those also ranked high in the agriculture study, with regulatory acceptable concentrations (RACs) OK as spelled out as regulatory acceptable concentrations? Abbreviation not used elsewhere. as assessment criteria (Holmes et al. 2018). The rankings according to exposure time also showed similar results. The rankings for chronic ecotoxic effects only (present results) identified chlorothalonil and cypermethrin as the first- and second-ranking compounds, which is also in line with the earlier study. For the chemicals emitted in the domestic scenario, the outcomes for galaxolide and ethinylestradiol co-rank high, although linear alkylbenzene sulfonate ranked lower in the MIXED scenario analyses than in the earlier scenario study (Diamond et al. 2018). For urban runoff, the top-ranked chemicals were deltamethrin, bifenthrin, permethrin, copper, and zinc, which also rank highly when assessed using landscape scenario analyses (De Zwart et al. 2018). In general, it can be stated that the prioritization options are many, that prioritization outcomes are dynamic in space and time, and, hence, that the problem definition phase should be used to define precisely which ranking information is most valuable for selecting an abatement option. Regulatory prioritization used to prospectively steer preventive policies can thus be different from more realized environmental quality-based rankings (Johnson et al. 2017).

Chemical footprints

The land-use scenarios were summarized as chemical footprints for direct, chronic risks for species assemblages. Chemical footprints were quantified using the P95 of the 7246 msPAF_{NOEC} outputs for each scenario (Table 4). A chemical footprint in this definition can be

used as management summary information; for example, when the $P_{95}\text{-msPAF}_{\text{NOEC}} > 0.05$, this means that for 5% of the days the (sub-)catchment outflow is ecotoxic such that the 95% protection level is exceeded, whereby a higher degree of exceedance of 0.05 implies a higher potential of the mixtures to affect species assemblages in the downstream water body. In other words, a chemical footprint of 6 for agriculture means that the 95% protection level is exceeded by a factor of 6 or more for 5% of the outflow days. The ecological implication of that depends on exposure time and downstream water body characteristics, although the chemical footprint signals “net outflow of toxicity.” In agriculture, chronic exposures were not found because of the swift effects of the flow regime. In a real system, though, chronic effects related to this chemical footprint may occur when chemicals would slowly accumulate in a water body, for example, in a lentic water body downstream of the outlet.

The chemical footprint results ranked the risks of mixtures as $\text{CITY} > \text{MIXED} > \text{agriculture}$ because of higher chemical footprint values and longer exposure durations. An additional scenario—agriculture along a river stretch with three 10-km² areas with nature downstream (agriculture–nature–nature–nature)—implied a reduction of the chemical footprint compared to agriculture only. For CITY the same layout did not reduce the chemical footprint substantially, related to the fact that the chemical footprint for the CITY scenario (0.95) is at the upper end of an exposure-mixture risk model which has a sigmoidal shape (like the underlying SSD model) so that a change in chemical emissions induced an equivalent reduction in chemical footprint. As an illustration of the option to evaluate abatement strategies, the bottom lines of Table 4 show changes in chemical footprint following from (imaginary) emission reductions for all chemicals by 25, 50, or 75%. The latter related to only a 47% lowered chemical footprint but an 80% reduction regarding exposure periods for the number of days with $\text{HI} > 1$ and 90% for the number of days on which $\text{HI} > 1$ was caused by one compound. The 75% abatement option quantified for the MIXED scenario implied that species assemblages at the catchment outflow experience lower exposure peaks, which are much less frequent and more often attributed to a single chemical.

DISCUSSION

Overview

The large number of chemicals detected in aquatic environments currently implies that there are large uncertainties regarding whether or not there is sufficient environmental protection against the adverse effects of individual chemicals and their mixtures. The number and diversity of mixtures in the environment seem to imply an intractable number of combinations of exposures, risks, and associated effects, as well as a remaining open end to the problem. This conundrum is often addressed using simplistic approaches (e.g., focusing on priority chemicals) that focus on protection but that ignore mixtures and that use assessment factors to account for the innumerable types of mixtures and uncertainties. However, despite the *in silico* approach of the present study, the results clearly indicate that the integrated assessment of numerous chemicals with different policy regimes (such as industrial chemicals and PPPs) and spatial–temporal exposure patterns is tractable. Further, the present study demonstrates an application of a strategic tiered approach, which provides refined ecotoxicological insights into the presence of risks for species assemblages (or even specific taxonomic groups, see Holmes et al. 2018). Therefore, the present study presents a testable framework designed to explore simplification and clarification of the spatiotemporal complexity of exposures and provides an approach for

forecasting risks based on scenarios created to capture the major influences on exposure for a given catchment or region. The study was based on 3 emission scenario assessments, built into a single approach to model emissions and risks at the scale of realistic combinations of subcatchments and land uses.

Comparison of predicted and observed parameters

A striking feature of the results was that the finding that the PEC variability resembled the observed ranges of the respective measured concentrations in river water samples (EMPODAT), despite considerable variation of modeled and measured data and technical limits regarding measuring compounds in field samples (Figure 3). The most striking observation was that the *in silico* modeled land-use scenarios (Figures 4 and 5) yielded an HI-MCR plot similar to that from a field study in which 12 to 81 PPPs were measured per sample (Vallotton and Price 2016; Figure 7), although the field study employed acute risk benchmarks (while we applied chronic ones). The difference between the present study and the agriculture study (Holmes et al. 2018) is caused by the use of regulatory acceptable concentrations to define mixture HIs in that study (this includes affected fractions of 100–1000 across compounds). Comparisons between predicted and observed data suggest that many of the findings of the present study can occur in true catchments. Therefore, the key patterns (below) bear relevant insights for assessing and managing complex mixtures in relation to land use.

Key patterns in the data

The similarities of exposures and hazard plots allow for some key observations.

First, land use matters. Land use appears to imply a typical chemical signature in receiving water bodies. A signature consists of a typical chemical composition (chemicals, concentrations) and exposure time aspects (durations, frequencies). Attempts to solve existing mixture exposures in aquatic systems could therefore focus on decoupling land use from aquatic systems, for example, via buffer zones, wastewater treatment, or reduced urban runoff emission events. Such actions would imply a change in emission of suites of chemicals, with those suites including the set of chemicals of high priority within the land use. Abating chemical risks can utilize a suite of options, not solely a chemo-centric approach (National Research Council 2009; Munthe et al. 2017); and it was, for example, shown earlier that an analysis of spatial associations between emission points and water bodies with sensitive functions (drinking water production, protected nature) can be a basis to reduce impacts via smart spatial arrangements (Coppens et al. 2015) and that clever strategies may be utilized to reduce adverse effects of chemicals and other water quality parameters (Malaj et al. 2014; Barclay et al. 2016). From upstream to downstream, land-use influences on smaller tributaries may be characterized by mixtures with greater exposures and simpler composition, with a “land-use dilution” effect in the downstream direction (López-Serna et al. 2012).

Second, flow and runoff events matter, related to rain events. Even though it was expected that domestic emissions would result in relatively constant exposures, the opposite is true in the smaller tributaries in our case. The results highlight the importance of rain events and subsequent dilution phenomena. Smaller rivers may be characterized by high temporal variability in chemical concentrations, whether or not there is a constant or an intermittent emission source (domestic vis à vis agriculture spraying/runoff and urban runoff runoff). Species in flowing aquatic systems can thus be exposed to mixtures that change rapidly in composition. A recent example (König et al. 2017) showed large changes of MECs of untreated wastewater emissions

in the Danube over a scale of a few kilometers only. Note that the PECs predicted for the subcatchments (current model) in reality could imply higher exposures at the points where true chemical emissions occur (e.g., edge-of-field exposures for agricultural chemicals and end-of-pipe exposures at wastewater-treatment plant outlets and sewer overflows). The spatial and temporal variation we modeled implies challenges for the design of monitoring schemes for flowing waters and indicates that spatiotemporal variation may disturb a straightforward interpretation of MEC data vis à vis the regulatory standards such as AA-EQS (Holt et al. 2000). For example, there may be doubts whether the MECs of a set of water samples are “representative” for the system, given spatiotemporal variability that may be an order(s) of magnitude. Modeling can help to improve understanding of the mixture risks of such systems.

Third, the choice of the assessment benchmarks matters. The integrated scenario analyses differ in this respect from the individual scenario studies (Holmes et al. 2018; Diamond et al. 2018; De Zwart et al. 2018), where various toxicity standards were used (see also Table 1). The uniform use of AA-EQS values in the present study resulted in a large number of days triggering regulatory concern, whereas inspection of the ecological implications of direct effects of mixture exposures (chronic or acute) showed substantially lower fractions of samples potentially causing direct effects on species assemblages (related to both peak exposures as well as nonchronic exposure times). This difference shows that it is important not to overinterpret criteria exceedances, such as the PNEC or the AA-EQS. The exceedance of such a criterion triggers regulatory concern, which should be translated into more specific information on the potential occurrence of direct ecological effects, secondary poisoning effects, or human health concern or into a trigger to improve the EQS itself when the affected fraction for one or more compounds is high. Avoiding misinterpretations has been proven useful for water quality management (Henning-de Jong et al. 2009).

Fourth, prioritization choices matter. Prioritization helps in selecting of cost-effective abatement strategies. A suite of prioritization options can be envisaged, and these result in vastly different lists of compounds for further attention (Guillén et al. 2012). The present study shows the effects of prioritization choices. Relevant information can be obtained from comparing land uses (clear ranking), exposure types (chronic or intermittent), and chemicals within mixtures. The latter is often used in practice, relating to the current identification of priority hazardous substances and substances prioritized for adoption on a “watch list” (regulatory attention triggered [European Commission 2013]). The observation of land use-specific chemical signatures suggests that chemicals that rank high in priority may serve as surrogates of co-occurring, nonmodeled, or measured substances (Bradley et al. 2017). Regulatory priority substances may be indeed prioritized but may also be of marginal importance for a catchment. Of the modeled compounds cypermethrin is a priority substance for European water policies and ethinyl estradiol is identified as a candidate for the watch list (European Commission 2013). In the present study, we found various substances ranking high in various ways which are not prioritized or watch list chemicals in the context of current regulation (European Commission 2013), for example, deltamethrin, permethrin, bifenthrin, galaxolide, sulfomethoxazole, caffeine, carbamazepine, pendimethalin, flufenacet, mesosulfuron-methyl, and fluoxastrobin. Regulatory attention may be warranted beyond regulatory lists, in line with other categorization options (Götz et al. 2010). River basin management is likely served best by a critical application of prioritizations, looking at land use, temporal aspects, chemicals of generic interest (e.g., at the European scale), and chemicals of interest given land-use practices. For a subcatchment, listed priority compounds may pose negligible risks within a given catchment and, conversely,

nonlisted compounds may be of high local priority for management. Neglect of compounds because of absence from a central listing can be called a case of unjustified reification. Reification is the process through which concepts (such as “priority compounds”) are increasingly interpreted as facts. Reification fallacies may seriously affect policy making (Bradbury 1989; Hyman 2010). Unjustified interpretations can induce type I errors (risk signals triggering abatement costs, without the signal being related to true impacts [Prato et al. 2014]) as well as type II errors (the potential impacts of many chemicals and their mixtures are neglected or remain unknown because of limitations of current science).

Fifth, the analyses always resulted in a clear identification of some chemicals contributing most to risks in mixtures. This phenomenon seems to be universal in field-related mixture studies, as substantiated by a variety of other assessments (Zijp et al. 2014; Vallotton and Price 2016; Backhaus and Karlsson 2014; Gustavsson et al 2017; De Zwart 2005; Harbers et al. 2006; see also Figure 7). The outputs of the present study suggest strong simplifying patterns of risk in highly diverse sets of mixture exposures. Land use–related chemical signatures appear to exist, whereby mixture effects are commonly caused by a few chemicals (for a given toxicological endpoint), although those few chemicals differ with land use and time (Munz et al. 2017).

Sixth, the reporting of findings as chemical footprint information summarizes the data for an area in easily understood metrics: the multiplication factor that mixture toxic stress of a sample exceeds a benchmark, which can be interpreted as a measure of the number of times a sample needs to be diluted before the effects are below the benchmark. In this evaluation, the dilution factors needed for the different land-use scenarios were 6, 19, and 9 for agriculture (realistic winter wheat scenario), a city (10 000 people/10 km²), and a mixed–land use scenario (Figure 1) to yield 95% of the species protected against NOEC exceedance because of mixture exposure for 95% of the days. Note that, commonly, various fate processes that we did not model may lower exposures in field conditions, which likely results in lower risks and chemical footprints. The predicted chemical footprint values are in line with other chemical footprint analyses for Europe (Zijp et al. 2014; Bjørn et al. 2014). In addition, the change in chemical footprint can be determined for varying catchment configurations (of urban runoff+domestic, agriculture, nature), and the effects of abatement options on the footprint can be explored (Table 4). Such summaries enable exploratory investigations as to the ecological risk reduction of altering landscape structure or impacts of alternative chemicals used for specific goals (e.g., choice of PPPs) or of chemical-specific or generically effective abatement strategies, such as buffer zones (Van Wezel et al. 2017).

Further analyses

Further data analyses are possible, for example, investigating which taxonomic groups are likely to be most affected by mixtures, checking time-weighted averaged exposures and the effects of the rainfall threshold causing city runoff, and analyses based on measured efficacies of, for instance, buffer zones between human activities and water systems. The refinement for taxonomic groups was already worked out in detail for the water samples of MCR group IIIB of the agriculture scenario (Holmes et al. 2018). Such analyses can refine insights into potentially sensitive groups. Because this effect is most prominent for the agriculture scenario and the original scenario study presents such outcomes in detail, we refer to that study for details of this kind (Holmes et al. 2018).

CONCLUSIONS

Based on the conceptual and practical evaluation of an integrative scenario, blending earlier reviewed agriculture, domestic, and urban runoff scenario data and acknowledging the limitations of this purely in silico study, we conclude the following. 1) It is possible to create a catchment-oriented approach, encompassing land use–related emissions of chemicals, rain events, and hydrological phenomena, to predict likely chemical profiles in receiving river catchments: the PECs generated by this approach bear a reasonable relationship with measured concentrations of chemicals and the predicted patterns of ecological risks, regarding both their magnitude as well as their maximum cumulative ratios, bear a reasonable resemblance to the pattern based on field data. 2) The land use–based approach, with realistic rain events and flow variation, results in highly variable mixture compositions in space and time (composition and concentrations of chemical mixtures) but also in simplified signatures and prioritizations. 3) The outcomes demonstrated spatiotemporal variability of exposure and potential ecological impacts of chemical mixtures in human-dominated systems but also allowed for simplifying generalizations, such as the potential for various meaningful prioritizations for risk management. 4) The complexity of 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 (in the present study dominated by agricultural, urban, and domestic wastewater-treatment inputs), but this requires developing "road map" scenarios with typical exposures for prospective and retrospective risk assessments and linking to management actions. 5) The varying exposure patterns can be described across ecosystem and land-use types by converting loadings to environmental concentrations in time-varying river flows and finally ecotoxicologically relevant endpoints, such as HQs and HIs and mixture toxic pressures, that can be related in a tiered way to expected net mixture impacts. 6) The explanation of outcomes of modeled or measured water quality assessments requires specific attention, to avoid overinterpretation of lower-tier methods. 7) The proposed approach for evaluating chemical mixture risks has a wide range of potential regulatory applications where approaches to mixture risk assessment are needed.

Supplemental Data—The Supplemental Data are available on the Wiley Online Library at DOI: 10.1002/etc.3960.

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

Data availability—Data, associated metadata, and calculation tools are available from the corresponding author (Leo.Posthuma@rivm.nl).

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Figure Captions

Figure 1. The MIXED land-use scenario layout of 10 subcatchments of similar size (10 km² each) in a total catchment of maximally 100 km². Water flows from the top of the figure to the bottom. **(A)**: Scenario definition table, defining the catchment, with land use and associated emission types. Bottom: Resulting catchment map with position codes (related to lag times of flow, **(B)**) and land-use codes **(C)** as defined in the scenario definition table. The different color intensities of the subcatchments indicate various hydrological travel times to reach the main catchment outlet, which enables modeling of time-dependent chemical fate processes. Other scenarios can be defined via entering codes for the lag times of the land uses in the scenario definition table. AGR = agriculture; DOM = domestic; NAT = nature; URB = urban runoff.

Figure 2. Illustration of the temporal variability of predicted environmental concentrations for 2 substances of the agriculture scenario: boscalid **(A)** and pendimethalin **(B)**, one for the domestic scenario: ibuprofen **(C)**, and one for the urban runoff scenario: fluoranthene **(D)**. AGR = agriculture; DOM = domestic; URB = urban runoff.

Figure 3. Comparison of measured environmental concentrations (MECs) of surface water systems, summarized as P5, P50, P95, and P99.9, of samples with a detectable concentration (greater than the limit of quantification in the monitoring data) and predicted environmental concentrations (PECs), summarized as P95 at the outflow of a subcatchment. Gray bars, MECs (darkening gray tones from low to high percentiles of detectable MECs); white and black bars,

PECs of subcatchments with a single land use and the MIXED scenario, respectively. The P99.9 percentiles are added to demonstrate the magnitude of peak concentrations within the series of 7246 daily PECs per scenario. The flow P99.9/P5 ratio is added to illustrate the magnitude of dilution (PEC) variation related to flow. AGR = agriculture; DOM = domestic; URB = urban runoff. **Please add A, B, and C designations to Figure 3 caption, I am not sure the best place to incorporate labels.**

Figure **Typesetter: Figure 4A: Please change 20 years to 20 yr**. Judgment of the 7246 hazard index (HI)-maximum cumulative ratio data points for predicted mixtures at the outlet of the whole 100-km² catchment, according to the land-use scenario depicted in Figure 1, evaluated by a generically protective regulatory criterion, the annual average environmental quality standard, to define the HI—for all dates (**A**) and for a single (randomly selected) year (**B**). Note: On the left some extremely high HI data points are not shown (see text). AA-EQS = annual average environmental quality standard; MCR = maximum cumulative ratio; RQ = risk quotient.

Figure **Typesetter: Figure 5A: Please change 20 years to 20 yr**. Judgment of the 7246 mixtures at the outlet of the whole 100-km² catchment, according to the land-use scenario depicted in Figure 1, judged by compound-specific hazard quotients derived from the 5th percentile of species sensitivity distribution (SSD) no-observed-effect concentrations (**A**) and the 50th percentile of SSD median effective concentrations (**B**)—for all dates (**C**) and for a single (randomly selected) year (**D**). EC50 = median effective concentration; HI = hazard index; MCR = maximum cumulative ratio; NOEC = no-observed-effect concentration; RQ = risk quotient; SSD = species sensitivity distribution. **Please check that I have the A,B,C,D designations correct in Figure 5.**

Figure 6. Tier-3 analyses of mixture impacts in scenarios with (A) land use agriculture and CITY (domestic+urban runoff) and (B) the MIXED scenario of Figure 1. The dotted line at multisubstance potentially affected fraction no-observed-effect concentration (msPAF_{NOEC}) = 0.05 is the 95% protection criterion, which was originally used in the derivation of predicted-no-effect concentrations for individual compounds. Water samples positioned right of the dotted line are mixture exposures at a level that, if exposure is indeed chronic, induces chronic effects to the fraction of species indicated on the x axis. AGR = agriculture; MCR = maximum cumulative ratio; msPAF = multisubstance potentially affected fraction; NOEC = no-observed-effect concentration.

Figure 7. Overlay of the hazard index-maximum cumulative ratio plots of 4380 measured concentrations of plant protection products in US watersheds (Vallotton and Price 2016) and of 7246 daily samples with associated predicted environmental concentrations from the agriculture subcatchment. Hazard indices were based on acute aquatic benchmarks for ecotoxicological effects and on the 5th percentiles of the species sensitivity distribution no-observed-effect concentrations, respectively, with the latter representing a more sensitive endpoint. Black dots indicate field data; white dots indicate current model results. HI = hazard index; MCR = maximum cumulative ratio.

ENOTE AQ10: “LAS” OK as spelled out as Linear alkylbenzene sulfonate

ENOTE AQ11: “HHCB” OK as spelled out as 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8,-hexamethyl-cyclopenta[g]benzopyran

Table 1. Characteristics of the original land-use scenario studies (Holmes et al. 2018, Diamond et al. 2018, De Zwart et al. 2018) and evaluations based on a subcatchment area of 10 km²

	Agriculture	Domestic	Urban runoff	Nature
Emissions	Rain event and PPP use-related (discontinuous, PPP use related to crop type)	Household-related (continuous, household chemicals, WWTP-chemical removal efficacies in Supplemental Data, Table S1)	Rain event-related (discontinuous, from wearing of buildings, brake pads, oils, etc.)	None
Emissions source	13 PPPs applied annually to winter wheat	Typical no. people/area, (10 000 inhabitants) Water use 200 L/person/d Effluent flow 0.0231 m ³ /s	Runoff, occurring at >10.3 mm rainfall/d (P95 of rainfall)	None
Chemicals	Boscalid Chlorothalonil Cypermethrin Epoxiconazole Flufenacet Fluoxastrobin Iodosulfuron-methyl Mesosulfuron-methyl Pendimethalin Prochloraz Proquinazid Prothioconazole Pyraclostrobin	1-OH-Benzotriazole Acesulfame Benzalkonium chloride Caffeine Carbamazepin Erythromycin Sulfomethoxazole Ethinylestradiol HHCB (galaxolide) Ibuprofen Linear alkylbenzene sulfonate Methylisothiazolinone TiO Zinc acetate Zinc oxide	Aluminium Benz[<i>a</i>]anthracene Bifenthrin Copper (dissolved) Deltamethrin Fluoranthene Iron (dissolved) Nonylphenolmonoethoxylate Permethrin Zinc (dissolved)	
Benchmark for PECs	Tier 1: RAC Tier 2: RAC species groups	Tier 1: PNEC Tier 2: PNEC of species groups	Tier 1: median EC50 (all species)	
Assessing mixtures	$\sum \text{PEC}/\text{RAC}^a$	$\sum \text{RCR}^a$	$\sum \text{RC}^a$ msPAF _{EC50}	
Reference	Holmes et al. 2018	Diamond et al. 2018	De Zwart et al. 2018	

^a In the present study a predicted environmental concentration benchmark ratio is generally referred to as the hazard index.

EC50 = median effect concentration; HHCB = 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8,-hexamethyl-cyclopenta[*g*]benzopyran; PEC = predicted environmental concentration; PNEC = predicted-no-effect concentration, utilized in generic protective chemical regulations; PPP = plant protection product; RAC = regulatory acceptable concentrations for edge-of-field water bodies, utilized in PPP regulations; RCR = risk characterization ratio (similar to hazard index in the present study);

msPAF_{EC50} = multisubstance potentially affected fraction of species exposed beyond their EC50;
 WWTP = wastewater treatment plant.

Table 2. Definition of sample subgroups at the outlet of the (sub-)catchment, characterized by grouping the maximum cumulative ratios (Vallotton and Price 2016)

Group	Mixture risk (HI)	Individual risk (HQ)	MCR	Meaning
I	HI >1	Max HQ >1		Mixture presents potential risk already based on individual compounds
II	HI <1	Max HQ <1		Assessment does not identify a concern
IIIA	HI >1	Max HQ <1	MCR <2	Mixture risk arises only from summing individual substance risk, although the majority of the mixture risk is driven by one substance
IIIB	HI >1	Max HQ <1	MCR >2	Mixture risk arises only from summing individual substance risk, with overall risk driven by multiple components

I = hazard index; HQ = hazard quotient; MCR = maximum cumulative ratio.

Table 3. Prioritizations on land use, based on various options to define the mixture hazard index

Scenario	Mixture hazard index definition	Signal of	Group I	Group IIIA	Group IIIB	Σ Dates with mixture hazard index >1
AGR	AA-EQS	Regulatory concern	634	66	14	714
	5th percentile SSD _{NOEC}	Sublethal effects	110	46	35	191
CITY (URB+DOM)	AA-EQS	Regulatory concern	6836	0	355	7191
	5th percentile SSD _{NOEC}	Sublethal effects	6577	0	617	7194
MIXED	AA-EQS	Regulatory concern	4236	4	2710	6950
	5th percentile SSD _{NOEC}	Sublethal effects	2442	8	4261	6711
	50th percentile SSD _{EC50}	Species loss	0	0	7	7

A-EQS = annual average environmental quality standard; AGR = agriculture; DOM = domestic; EC50 = median effect concentration; NOEC = no-observed-effect concentration; SSD = species sensitivity distribution; URB = urban runoff.

Table 4. Scenarios summarized as chemical footprint indicators

Scenario	P95 msPAF _{NOEC}	Chemical footprint (multiplication factor the 95% protection level is exceeded)
AGR	0.30	6.0
AGR–NAT–NAT–NAT	0.14	2.8
CITY	0.95	19.0
CITY–NAT–NAT–NAT	0.93	18.8
MIXED	0.46	9.1
MIXED-abatement 25%	0.40	8.0
MIXED-abatement 50%	0.33	6.6
MIXED-abatement 75%	0.22	4.3

GR = agriculture; msPAF = multisubstance potentially affected fraction; NAT = nature; NOEC = no-observed-effect concentration.

SUPPORTING INFORMATION

PROSPECTIVE MIXTURE RISK ASSESSMENT AND MANAGEMENT PRIORITIZATIONS FOR RIVER CATCHMENTS WITH DIVERSE LAND USES

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Running Head:

Blending mixture exposure scenarios for risk assessment

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M&M: INTEGRATING LAND USE SCENARIOS

Land uses, geography and hydrology

Three separate chemical emission scenarios (Agriculture-AGR, Domestic-DOM, Urban-URB) along with no-chemical emission scenario (Nature-NAT) were developed on the basis of literature reviews and by combining hydrological- and ecotoxicological modelling techniques with various regulatory judgment criteria [1-3]. DOM and URB relate to the land use CITY. The scenarios were substantiated in a spreadsheet model for a catchment of 100 km², which can consist of one to ten sub-catchments of 10 km² each, linked in a river network. The spreadsheet is an expansion of the model described for the AGR-scenario [1]. Details are in that study. The characteristics that are relevant for the current study are described below.

In the spreadsheet, land use combinations can be varied by assigning the land uses to sub-catchments in a spatial arrangement. The position (p) of a sub-catchment relative to the main (100-km²) catchment outlet was defined by the number of days travel to the outlet (i.e., “lag” time), where p=0 (sub-catchment containing the main catchment outlet), p=-1 (sub-catchment one day from the catchment outlet), p=-2 (sub-catchment two days from the catchment outlet, see Figure 1 of the main paper).

The model contains baseline flow information for each sub-catchment land use type to represent the flow arising from realistic conditions relating to the selected soil characteristics, land area, water retention time, and river stretch dimensions. The flow data are dynamic, changing with rainfall events, and flow statistics can be summarized for the bottom of each sub-catchment, and be aggregated to the net outflow of the whole catchment.

Hydrology

The modeling framework for hydrology is based on the catchment model SWAT (<http://swat.tamu.edu/>), a model that is used to predict the effect of management decisions on water, sediment, nutrient and pesticide yields with reasonable accuracy on large, ungauged river basins. The inputs of surface runoff in this model are consistent with the model PRZM (<https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment>) with the Soil Conservation Services (SCS) Curve Number approach, which was used in the AGR scenario paper. SWAT scales up beyond the 1-ha field simulated for the AGR-scenario and it incorporates the effects of baseflow and runoff in urban areas.

SWAT was used to generate separate simulations for the three types of 10-km² sub-catchments: natural areas (land uses with no significant application of chemicals by man and therefore no significant emissions), agriculture, and city. The model was run for one soil type, taken from the EFSA FOCUS model (R1 scenario) and with curve numbers adjusted for natural, agricultural or urban land use.

Flow simulations were generated for the 20-year period (7246 days, March 1, 1975 to December 31, 1994) using the realistic rainfall data from the AGR scenario analyses [1]. A spreadsheet was used to combine the 10 km² outputs (daily loadings and flow) to ensure consistency with the loading approach, transparency, and scenario evaluations (e.g. impact of different proportions of each land use, or impact of an urban area being located at the top or bottom of the catchment).

The 20-year time period was modelled on a per-day basis, with historic rain events and associated flows. In addition to the hydrological model, the following details define the selected conditions in the model. The original AGR scenario calculations are characterized by a dynamic hydrology for a small, field-edge water body with emissions driven by pesticide applications (drift) or storm events (runoff). For this scenario (UK-winter wheat), daily loadings were obtained from the outputs of AGR-FOCUS runs (using PRZM and a spray drift calculator). Resulting values are relevant to 1-ha of wheat, combining spray drift and surface runoff loadings. These outputs were linearly scaled for the current study to loadings relative to the 10-km² sub-catchment using the proportion of wheat in the sub-catchment; for the illustrative simulations undertaken here, it was assumed that the entire 10-km² sub-catchment (i.e. 100% of the surface area) was cropped with winter wheat and treated with the pesticide program described in the AGR scenario analysis [1]. The original DOM-scenario generates constant concentrations in a large river defined to deliver a 10-fold dilution of concentrations leaving the wastewater treatment plant. For the integrated DOM-scenario, the loadings were determined for a population estimate for a 10-km² sub-catchment of urban/suburban area of 10,000. The loadings (mass) were back calculated from effluent-PECs based on effluent flow. Thereupon, the effluent loadings were scaled to the 10-km² population. The original URB-scenario was driven by information on chemical monitoring data (chemical identities and concentrations), while the frequency of contaminant emissions and scale of the receiving water body were not defined. For the integration of the URB-scenario in the current study, the aim was to obtain daily loadings at the base of the 10-km² sub-catchment. The 20-year rainfall data were used to determine the days when loadings occur due to stormwater runoff. Therefore, the daily rainfall amount on each 10-km² sub-catchment was examined, and a threshold was applied to determine whether urban runoff was triggered.

Land uses, chemical emissions and their assessment

2.3.1. General design and approach

The original agriculture scenario (UK winter wheat scenario, [1]) was used as basis for the catchment scenario spreadsheet model. This scenario considers twenty consecutive years, with realistic weather conditions (rain), the hydrological effects of which were modelled on a day-to-day basis for the sub-catchment flows. Here, concentrations of chemicals were calculated at sub-catchment outlets as derived from daily loadings and flow for each type of sub-catchment,

followed by dynamic calculation of the mixture concentrations at the bottom of the sub-catchments and the total catchment configuration. The resulting Predicted Environmental Concentrations at the (sub-)catchment outlet were judged via various methods, which were in part similar to the original scenario studies on AGR, DOM and URB, but also in part different. Some judgment criteria are specific to individual compound groups (such as e.g. the Regulatory Accepted Concentration, RAC, for edge-of-field risk assessment of plant protection products). Additional evaluation criteria were selected so as to allow for comparison across land use scenarios on a consistent basis.

2.3.2. Agriculture

Compounds. The selected agricultural land use scenario AGR is the original row crops scenario (winter wheat, U.K., [1]). The AGR scenario considers the typically used winter wheat plant protection product applications (substances, timings of use, amounts of use), applied according to defined agricultural practices. The study considers 13 active substances, applied annually over the 20 years, with application rates derived from actual use statistics. Emissions to water (loads) were those used in the original study.

Emissions. The FOCUS R1 runoff scenario was used in the original study to model chemical emissions. Cited from the detailed Supporting Information of that study [1]: “[It] comprised a free-draining light silt soil with small organic matter content (5% sand, 82% silt, 13% clay, 1.2% organic carbon) coupled with a temperate climate with moderate precipitation (600-800 mm annual average rainfall, 100-200 mm annual rainfall, 6.6-10 °C average temperature in autumn and spring), gently to moderately sloping land (2-4%) and a range of crop types including winter cereals that was simulated for the current purpose. Related to environmental fate parameters, half-lives for degradation in soil were selected from aerobic laboratory studies undertaken at 20°C and normalized to soil moisture content at pF2 (FOCUS 2000). The soil-water partition coefficients normalized to soil organic carbon content (Koc) and Freundlich exponent (nf) were selected from standard batch studies. Where the number of studies available exceeded four, standard regulatory practice was followed with the geometric mean of all available values as input to the model for degradation half-life and Koc and the arithmetic mean used for nf (FOCUS 2014). Generally, there were two natural water/sediment values available and here the arithmetic mean was taken for degradation in the water and sediment phases.” For the current study, the scenarios were based on 100% of AGR-land grown with treated winter wheat, and PECs at the edge-of-field was assumed to be equal to the PECs at the outlet of the sub-catchment (sorption/degradation during transport from point of emission to sub-catchment outlet is ignored, and travel times to the sub-catchment outlet are assumed to be <1day).

Evaluating risk. The judgment of PECs in the present study was made with various methods, harmonized amongst the land use scenarios, and (partly) different from the approaches in the original AGR scenario study. The methods are described in the main paper, and details are in Section S.I. 0. For the original AGR-study on winter wheat, risks were evaluated using Regulatory Acceptable Concentrations (RACs), evaluated at the edge-of-field scale water body. RACs are effects assessment endpoints expressed in terms of a permissible concentration in the environment that is directly used in the risk assessment by comparing it to the (predicted) aquatic exposure concentration. If the concentration is lower than the RAC, the environmental effects of a PPP are assumed to be acceptable and consequently the risk is deemed low. In the original

study, RACs were also calculated for taxonomic groups (i.e. fish, invertebrates and primary producers), using the available data and the methodology appropriate for an EU risk assessment of PPPs, applying the assessment factors according to the EFSA Aquatic Guidance (related to quantity and quality of available ecotoxicity data). Higher tier ecotoxicity data were also used, using the endpoints generally as presented in the respective EU assessments and following current EFSA guidance. The outcomes of the original AGR-study were based on various approaches, amongst which the RAC and cumulated RAC-ratios using the lowest value from all the taxonomic groups as Tier-1 approach, and taxonomic-group specific RACs as Tier-2 approach. The present study considers concentrations at the outlet of the AGR-sub-catchment, or at the outlet of the whole catchment of the scenario model run.

2.3.3. Domestic

Compounds. The original domestic scenario [2] considered nutrients, consumer products, pharmaceuticals, hormones, solvents and specialty chemicals. Emission sources were diverse, and the current study focuses on domestic emissions only. The emissions are considered to occur via point sources, and are related to population density and characterized by a continuous discharge, treated on a pathway including a waste water treatment plant (type modelled for the integration scenario: activated sludge). In the domestic scenario, typical household chemicals were selected for the exposure and risk modelling of the integration paper (with relatively high contribution to risks in the original scenario [2]).

Emissions. Domestic loadings were modelled using the following characteristics: 200 L of water use per day per capita, 10,000 people inhabiting the sub-catchment of 10 km², a WWTP-dilution factor of 10, a basic river flow of 0.231 m³/sec, and loading- and WWTP-removal efficiencies (activated sludge technique) as in

.I. Table 1. The loadings combined with the hydrological model yielded the PECs at the sub-catchment outlet. Note that the loadings are modelled as constant (per-capita constant use of household chemicals), while the hydrological dynamics result in time- and flow-dynamic PECs at the outlet.

Full name	Abbreviation used	Per capita use rate (g/cap/d)	Removal (Activated Sludge)	Effluent Mass Loading (g/d)
1-OH-Benzotriazole	D-BTZ	0.003	0.0%	30
Acesulfame	D-ACS	0.015	27.0%	109.5
Benzalkonium chloride	D-BAC	0.0082	99.8%	0.1632
Caffeine	D-CAF	0.30	84.0%	480
Carbamazepin	D-CMZ	0.0014	22.0%	10.92
Erythromycin Sulfomethoxazole	D-SMX	0.005	58.0%	21
Ethinylestradiol	D-EE2	0.0000018	82.0%	0.0032
HHCB (Galaxolide)	D-HHCB	0.02	56.0%	87.12
Ibuprofen	D-IBU	0.019	90.0%	18.55
LAS	D-LAS	0.60	99.0%	60
Methylisothiazolinone	D-MI	0.0006	50.0%	3
TiO	D-TiO	0.098	97.0%	29.25
Zinc acetate	D-ZnA	0.0032	74.0%	8.29

.I. Table 1. Details on the modelled data for selected chemicals from the domestic scenario (D=domestic).

Evaluating risk. The judgment of PECs in this study was made with various methods, harmonized amongst the land use scenarios, and (partly) different from the approaches in the original scenario studies. The methods are described in the main paper, and details are in Section S.I. 0. The Tier 1 assessment of PECs in the original study was based on predicted no effect concentrations (PNEC). These were derived as threshold values following the EU guidance [4] by applying assessment factors to the reported effect data and selecting the lowest value of the three species groups (fish, aquatic plant, and crustaceans) as the PNEC. The Tier 2 assessment of PECs in the original study consisted of the comparison of the chronic no effect concentrations of separate species groups, which were used as the threshold values. If chronic values were not available, acute values were used and divided by a factor of ten to extrapolate from acute to chronic effects. We acknowledge that for some chemicals, acute to chronic ratios may be much higher based on endocrine disruption effects. The Tier 2 differentiation between species groups provides enhanced diagnostic resolution and may allow identification of the species group(s) at greatest risk. It was noted that for ZnO, the Tier 1 threshold values reflect the toxicity of the Zn^{2+} ion, which is considered to cause the toxic effects. The Tier 2 threshold values for ZnO, and TiO are based on tests with nanomaterials, which are the actual ingredients of the sunscreen products. Risk Characterization Ratios (RCR) in the original study were computed based on PECs and the PNEC values obtained as described above. The RCRs for individual chemicals were then summed, providing a cumulative RCR (EC, 2003) as a measure for approximating the risk of the mixture for each treatment type, although it is acknowledged that this may imply aggregating very different PNEC-types. In the Tier 2 approach of the original study, a cumulative RCR was computed for three organism groups – fish, daphnia, and algae – separately. The aggregated values were named ‘hazard quotients’ (being cumulative RCRs) and were determined for each organism group. It was noted that the chronic toxicity values collected in Tier 2 were not necessarily the toxicity estimates on which the PNEC of Tier 1 was based.

2.3.4. Urban

Compounds. The original urban runoff scenario [3] considered PAHs, metals, and solids, and emissions of those compounds from sources such as roads, parking lots, buildings and roofs, in total 77 compounds. The available data concern defined amounts of runoff, typical event mean concentrations, defined flows in receiving waters, considering roads, buildings, parks, other structures, and hydrodynamics with intermittent exposures (rain events and run off), with industrial direct-, industrial indirect-, and domestic flowing into combined storm overflows. For the URB-modelling, a selection of the top 10 chemicals causing indications of risk were selected for the present study.

Emissions. Urban loadings were modelled in a dynamic way, but they were determined by a threshold rainfall event, which was set as the 95% percentile of the 20-year rainfall data (P95 = 10.3 mm rainfall). With an altered threshold event, the urban runoff will be more frequent with lower loads (lower threshold), or less frequent with a higher load (higher threshold). The selected

threshold represents expected runoff loads and PECs as in the URB scenario paper, based on 30% land area being impervious surface connected to a drain system. In this way, a sufficient amount of rainfall in an event generates runoff and associated runoff PECs. To derive PECs from the loading events, 30% of the land area was assumed to consist of impervious surface connected to drain system, and therefore 30% of the runoff water volume was assumed to reach the water body. Data are in S.I. Table 3.

Full name	Event Mean Concentration in runoff water (g/m ³)	Mass loading (g/d) for runoff volume of 3.06E+04 m ³ /day
Copper dissolved	0.033	1.01E+03
Zinc dissolved	0.084	2.57E+03
Deltamethrin	0.000084	2.57E+00
Bifenthrin	0.00003	9.18E-01
Benz(a)anthracene	0.000192	5.88E+00
Permethrin	0.000202	6.18E+00
Iron dissolved	1.106	3.38E+04
Aluminum reactive	0.0242	7.41E+02
Nonylphenol ethoxylate	0.004165	1.27E+02
Fluoranthene	0.000887	2.71E+01

S.I. Table 3. Details on the modelled data for selected chemicals from the urban scenario for a 10.3 mm rainfall event.

Evaluating risk. The judgment of PECs in this study was made with various methods, harmonized amongst the land use scenarios, and (partly) different from the approaches in the original scenario studies. The methods are described in the main paper, and details are in Section S.I. 0. In the original study, the PECs were judged using the median EC50 of the data set of all species, and by the mixture toxic pressure, calculated via SSD_{EC50} models (msPAF_{EC50}).

M&M: EVALUATING RISK

On the existence of various benchmarks

The original studies [1-3] apply various toxicity benchmarks (BMs) to judge the PECs and the mixtures at the outlets of the (sub-)catchments. The judgment criteria differed vastly across the three studies, as they were selected in the original studies in relation to the pertinent regulatory context, e.g., generic environmental assessments, or species assessments for plant protection products. In the present study we applied several benchmarks in a similar way across the land uses, to avoid repetition and to align the AGR-study to the judgment options for the other land uses and substances.

On the benchmarks used in the present study

The specific judgment criteria in the current study were:

- For individual chemicals:

- A regulatory benchmark concentration, AA-EQS, the Annual Average Environmental Quality Standard, as applied in the context of the European Water Framework Directive [5]
 - A scientific benchmark concentration representing the concentration at which it is predicted that 5% of the species would be affected beyond their NOEC, abbreviated as the 5th percentile of an SSD_{NOEC}; this value is also known as the HC5, the Hazardous Concentration for 5 percent of the species based on an SSD_{NOEC} [6], and it is interpreted often as the so-called 95%-protection level (95% of the species is protected against direct adverse effects of exposure on endpoints such as growth and reproduction)
 - A scientific benchmark concentration representing the concentration at which it is predicted that 50% of the species would be affected beyond their EC50, abbreviated as the 50th percentile of an SSD_{EC50}
- For mixtures: the multi-substance toxic pressure, quantified as the chronic msPAF_{NOEC} and the acute msPAF_{EC50} in line with the models underlying the two scientific benchmarks [7], see also S.I. Section 0.

On the tiers of the HI – MCR assessments in the present study

The HI-MCR plotting method [8] was applied to summarize the data of a scenario run (for a specific sub-catchment, or for the multiple land uses scenario) using different benchmark definitions, representing different tiers. A choice for another benchmark influences the position of each HI-MCR data point (modelled day) both for the HI (X-position) and the MCR (Y-position).

2.3.5. Tier 1: AA-EQS

In Tier 1, the HI-MCR plots were made by defining compound-specific-HQs via regulatory protective environmental quality standards (EQSs). Generic EQSs are commonly used as regulatory criteria for water quality assessments. These EQSs are typically derived as concentrations below which negligible adverse effects occur via direct and/or secondary

exposure effects on ecological structure and function, or they represent negligible effects on human health. The lowest of these critical concentrations (ecological, human health) is used as a generically protective EQS. In its derivation – to be protective also under uncertainty – a generically protective EQS is often derived by applying an additional application factor (AF) to output of weighing the available effect data. The AF serves to guarantee sufficient protection also when effect data for deriving the standard are poor, and the magnitude of the AF is thereby dependent on the amount and quality of the input data for an endpoint (higher uncertainty → higher AF → lower EQS). As different jurisdictions have different EQS-definitions, we harmonized the approach by only using EU criteria. These are the PNEC and the AA-EQS and MAC-EQS (annual-average EQS, and maximum acceptable concentration EQS). Generic PNECs and AA-EQS and MAC-EQS were obtained from RIVM's website (<http://www.rivm.nl/rvs/>).

It should be noted that, given this way of benchmarking, the EQSs for two compounds A and B can be based on different endpoints (e.g., biodiversity protection for compound A and human health for compound B) so that the HI can be numerically quantified as the sum of the HQ-A + HQ-B, while this value has no meaningful biological interpretation. Moreover, due to the use of the various AFs across compounds, the value of a HQ can become (very) high (e.g., when an EQS is slightly exceeded, while it was derived with an AF of e.g. 100 or 1000). High HI-values in Tier 1 signal regulatory concern, but can – for the above reasons – be refined as to which endpoint may be affected most (ecosystems, human health) in which way (direct effects, secondary poisoning, specific endpoints), or whether there are high uncertainties contributing to the concern-signal (one or more compounds with high AF).

2.3.6. Tier 2: Quantifying benchmarks for effects of mixture exposure on species assemblages

To address the weaknesses associated to the Tier 1 approach, a Tier 2 method was used in which analyses were made using ecotoxicological effect-based criteria concentrations (EBC) without AFs, similar to analyses of Malaj et al. [9].

Tier-2 values were summarized as HQ_{EBC} and HI_{EBC} , with values >1 indicating that chronic or acute effects on growth and reproduction are likely within the exposed species assemblage for EBCs. This was done using EBCs based on NOECs and EC50s respectively. HI-values were derived from linear summation of HQ-values, which utilizes a linear concentration-effect model concept (per compound) and concentration addition modelling (aggregating compounds). The benchmark values themselves were derived on the basis of Species Sensitivity Distribution (SSD) models for chronic and acute endpoints from SSD_{NOECs} for chronic- and from SSD_{EC50s} for acute impacts (see S.I. Section 0). The parameters of the underlying Species Sensitivity Distribution models (SSD_{NOEC} and SSD_{EC50}) are provided in S.I. Table 4. $HI_{NOECs} >1$ and $HI_{EC50s} >1$ were interpreted as indicators of direct chronic, sublethal ecological impacts of the mixtures at the (sub-)catchment outlets on species assemblages and as a species loss from exposed assemblages, respectively.

2.3.7. Tier 3: Quantifying mixture toxic pressures

Third, a Tier-3 refinement was made by quantifying the chronic and acute mixture toxic pressures ($msPAF_{NOEC}$ and $msPAF_{EC50}$) for the 7246 daily sample days of a scenario run. In contrast to the Tier-2 approach, the $msPAF$ -outputs are characterized by an upper limit of the

predicted impact on species assemblages, i.e., at maximum, 100% of the species in an assemblage are predicted to be affected at the modelled endpoint.

On SSD-models and mixture toxic pressures

Effect-Based Criteria (previous section) and mixture toxic pressures were calculated using Species Sensitivity Distribution (SSD) modelling, starting from EC50-based SSDs [10].

Mixture toxic pressures were calculated for all daily predicted samples at (sub-)catchment outlets. This was done using an average SSD-slope for all compounds, derived from the SSD-models for which sufficient data were available (see [11]). The mixture toxic pressure was thereupon quantified assuming concentration additivity across all compounds modelled in a land use scenario. The application of this approach is in line with the assumption utilized for the HI approach used in the Tier-1 and Tier-2 risk characterization approaches of this study, and we note that the quantitative error that might be introduced as compared to the mixed-model approach (assuming within-compound group concentration additivity, and across-compound groups response additivity) is commonly small [12]. SSD_{EC50}-models were derived from downloaded ecotoxicity data. Details are in S.I. Table 4. Due to the presence of clear patterns across SSD_{EC50} and SSD_{NOEC} [11] it was also possible to extrapolate SSD_{NOEC}s from the tabulated data, and to derive the mixture toxic pressures at the NOEC level. In short, the outputs of mixture toxic pressure models were derived to represent the fraction of species affected beyond their NOEC, which we characterize as experience discomfort at chronic exposure, and the fraction of species affected beyond their EC50, which is a fraction found to associate to species loss [13].

ChemName	AvgToxicity(ug/l)	10LogAvgToxicity(ug/L)	#ToxDat	#Species	#TaxClass	QualityScore	Remarks
1-OH-Benzotriazole (BTZ)	758.58	2.88	14	14	3	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Acesulfame	1000000.00	0.70					Via MOA extrapolation and common slope of SSD: 10LogSlopeSSD(mol/m3)=0.7)
Aluminium	2242.33	3.35	30	11	4	41	Lumped data - Officially enough species (>10) for ERA with SSDs
Benz(a)anthracene	9.66	0.99	8	7	5	42	Lumped data - Enough species (6-10) for ERA with SSDs
Benzalkonium chloride (BAC)	1759.95	3.25	12	4	2	43	Lumped data - marginally enough species (3-5) for ERA with SSDs
Bifenthrin	1.04	0.02	50	24	4	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Boscalid	2874.09	3.46	11	11	7	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Caffeine	16538.65	4.22	17	7	5	12	Extrapolated from Acute NOEC - Enough species (6-10) for ERA with SSDs
Carbamazepin	38743.60	4.59	52	19	12	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Chlorothalonil	103.32	2.01	178	66	15	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Copper (dissolved)	183.78	2.26	116	71	14	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Cypermethrin	0.77	-0.11	186	84	8	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Deltamethrin	1.97	0.29	177	62	7	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Epoxiconazole	541.50	2.73	19	12	6	31	Extrapolated from Chronic NOEC - Officially enough species (>10) for ERA with SSDs
Ethinylestradiol	1905.90	3.28	16	13	5	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Flufenacet	3879.72	3.59	8	6	3	2	Not extrapolated - Enough species (6-10) for ERA with SSDs
Fluoranthene	135.58	2.13	36	30	12	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Fluoxastrobin	700.16	2.85	25	16	6	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
HHCb (Galaxolide)	1000.00						Via MOA extrapolation and common slope of SSD: 10LogSlopeSSD(mol/m3)=0.7)
Ibuprofen	20304.86	4.31	46	20	9	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Iodosulfuron-methyl	26169.78	4.42	10	10	6	2	Not extrapolated - Enough species (6-10) for ERA with SSDs
Iron (dissolved)	25234.81	4.40	23	7	4	42	Lumped data - Enough species (6-10) for ERA with SSDs
Linear alkylbenzene sulphonate (C1)	3224.78	3.51					
Mesosulfuron-methyl	4412.66	3.64	19	16	6	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Methylisothiazolinone	188.71	2.28	7	3	2	43	Lumped data - marginally enough species (3-5) for ERA with SSDs
Nonylphenolmonoethoxylate	7353.60	3.87	26	19	4	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Pendimethalin	951.48	2.98	62	31	9	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Permethrin	12.12	1.08	314	104	10	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Prochloraz	1006.00	3.00	45	16	6	31	Extrapolated from Chronic NOEC - Officially enough species (>10) for ERA with SSDs
Proquinazid	100.00						Via MOA extrapolation and common slope of SSD: 10LogSlopeSSD(mol/m3)=0.7)
Prothioconazole	1436.81	3.16	13	11	6	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Pyraclostrobin	20.71	1.32	14	8	5	2	Not extrapolated - Enough species (6-10) for ERA with SSDs
Sulfamethoxazol	9444.96	3.98	45	15	8	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Titanium oxide (TiO2)	18535.32	4.27	47	12	9	11	Extrapolated from Acute NOEC - Officially enough species (>10) for ERA with SSDs
Zinc (dissolved)	1852.68	3.27	52	45	12	1	Not extrapolated - Officially enough species (>10) for ERA with SSDs
Zinc acetate	1627.80	3.21	7	7	4	2	Not extrapolated - Enough species (6-10) for ERA with SSDs
Zinc oxide	8568.41	3.93					Not extrapolated - Officially enough species (>10) for ERA with SSDs

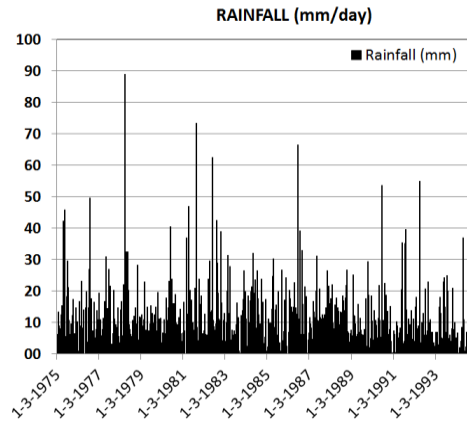
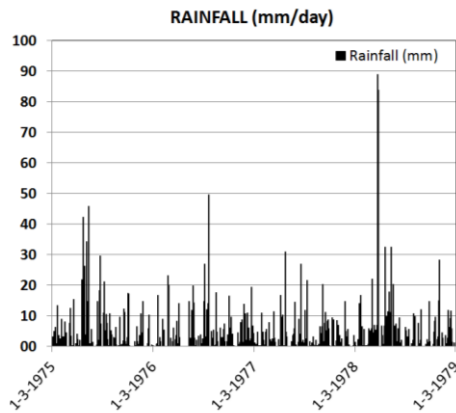
S.I. Table 4. SSD_{EC50}-parameters. AvgToxicity=Average toxicity value (EC50). #ToxDat=number of input data utilized to derive the SSD. #TaxClass: number of taxa in

the SSD data set. Quality score: lowest score=1 indicates a direct derivation of an SSD_{EC50} from the data. Higher quality score numbers imply the presence of (coded) extrapolation or interpolation steps, and/or less reliable fit of SSD-model to the data due to a low number of input data, see next column for explanation. E.g., “quality score 41” means that data of various types are lumped via acute-chronic extrapolation, and collated into the SSD_{EC50} .

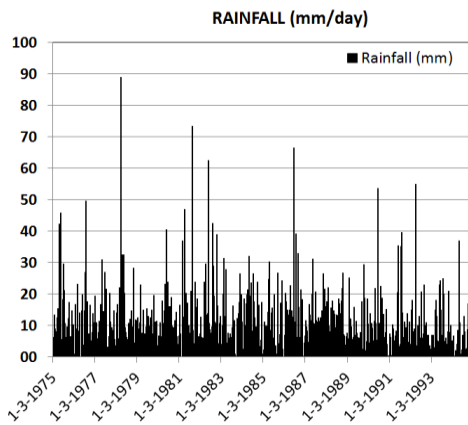
RESULTS: PHYSICO-CHEMICAL RESULTS

Rainfall

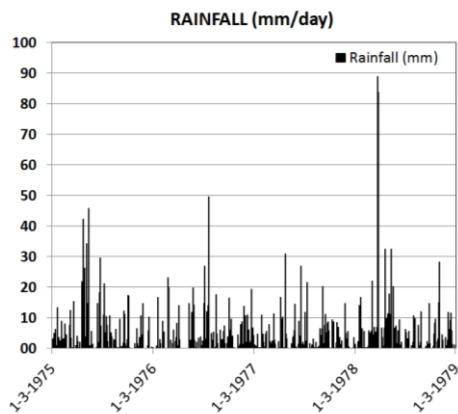
Rainfall data are summarized in



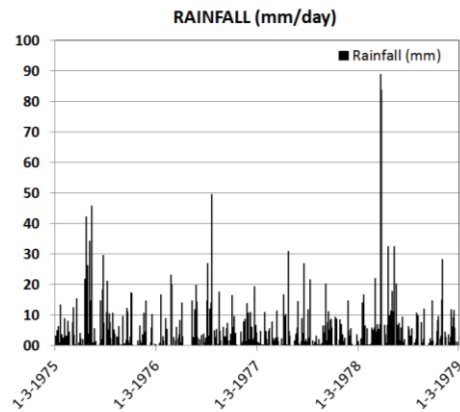
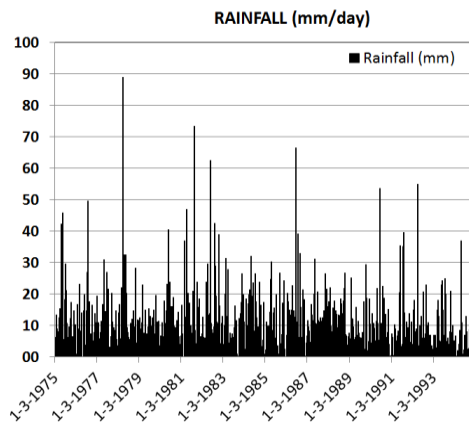
S.I. Figure 1, for 7246 consecutive days. Source data are rain events data associated with the FOCUS R1 exposure scenario from a European weather station, for the period of March 1, 1975 to December 31, 1994.



INSERT



S.I. Figure 1 HERE

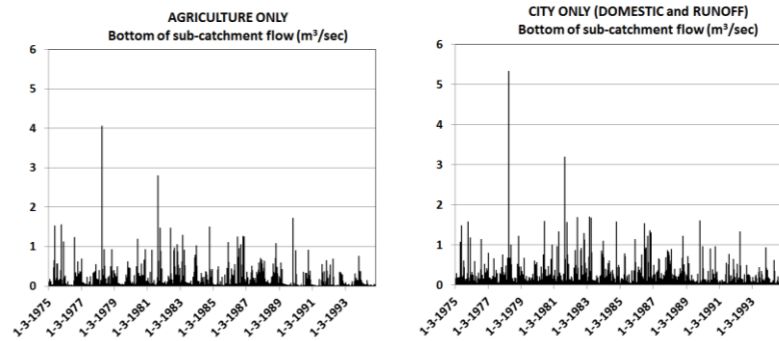


S.I. Figure 1. Rainfall. Left: for the whole period. Right: detail of rain events, for a selected period.

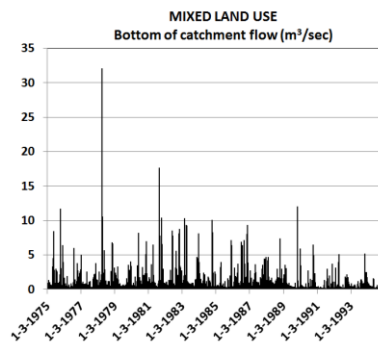
The natural rainfall was summarized as percentiles (P5, P25, P50, P75, P95, P99.9) for 7246 days as 0, 0, 0, 2, 10 and 53 mm.day⁻¹, which implies high variability over time. This resulted in a variation of flows, and thus predicted dilutions of chemicals (see below for PECs, see SI Figures 1 and 2 for rainfall and flow details). For a CITY sub-catchment (DOM+URB), the flow

percentiles were 0.03, 0.04, 0.06, 0.10, 0.35 and 1.70 $\text{m}^3.\text{sec}^{-1}$ (which includes the municipal wastewater effluent discharge for 10,000 people at 200 L/day ($0.0231 \text{ m}^3.\text{sec}^{-1}$, see main paper)). For an AGR sub-catchment, the flow values were 0.005, 0.02, 0.04, 0.07, 0.29, and 1.63 $\text{m}^3.\text{sec}^{-1}$, which was slightly lower than for CITY. For a NAT sub-catchment, the values were 0.01, 0.03, 0.05, 0.07, 0.22, and 1.24 $\text{m}^3.\text{sec}^{-1}$. For the MIXED land use catchment, the values were 0.08, 0.14, 0.31, 0.51, 0.84, 2.61 and 13.32 $\text{m}^3.\text{sec}^{-1}$.

Flow

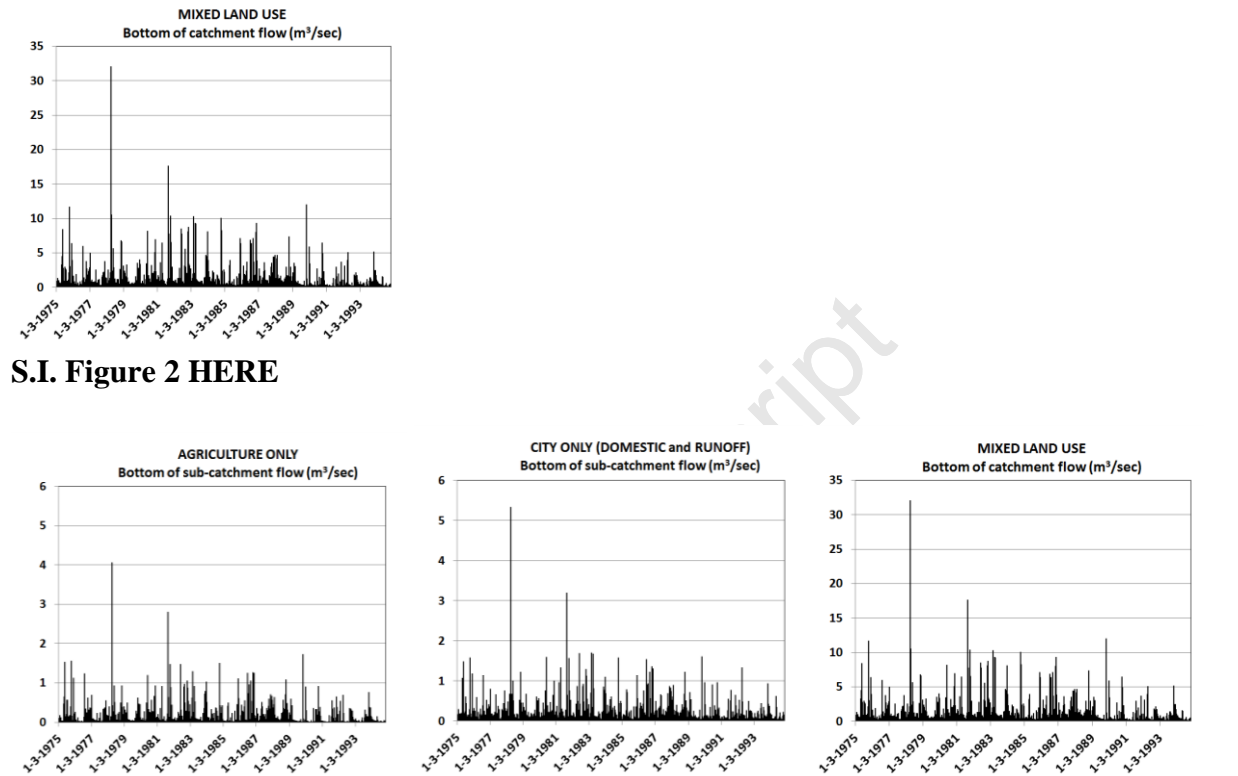


Flow data are summarized in



S.I. Figure 2, for 7246 consecutive days. The hydrological effects of the rainfall events differ for the different land uses, modelled here as AGR-sub-catchment and a CITY sub-catchment (with the DOM and URB scenario outputs combined along with DOM effluent), as well as for the MIXED land use for the whole catchment (see Figure 1 in main paper for MIXED catchment configuration used in this scenario).

INSERT



S.I. Figure 2 HERE

S.I. Figure 2. Illustration of flow data variability over time and across land use scenarios. Example scenarios are 10 km² AGR scenario in one sub-catchment (left), 10 km² CITY scenario in one sub-catchment (with DOM and URB emissions, middle), and the 100 km² mixed-land use scenario of Figure 1 of the main paper. (with CITY, AGR and NAT land uses, right).

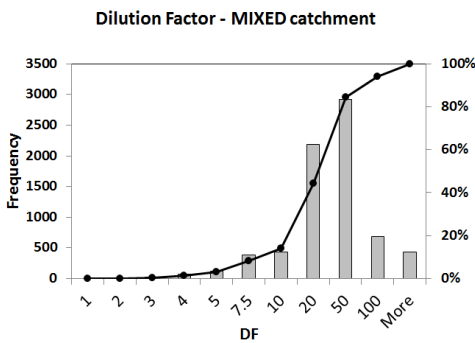
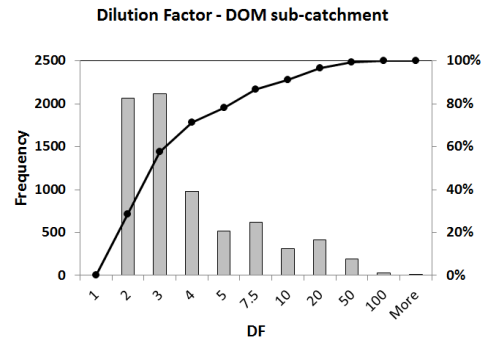
As flow variation implies chemical dilution variation, we illustrate the magnitude of the flow variability with P99.9/P5 flow ratios. High-low flow ratios were 55, 324, 128 and 94 for the scenarios CITY, AGR, NAT, and MIXED, respectively. This suggests different flow and dilution dynamics in the different sub-catchments (land uses), with large (rain- and runoff related) temporal effects superimposed on relatively lower spatial (land use) effects.

Effluent dilution

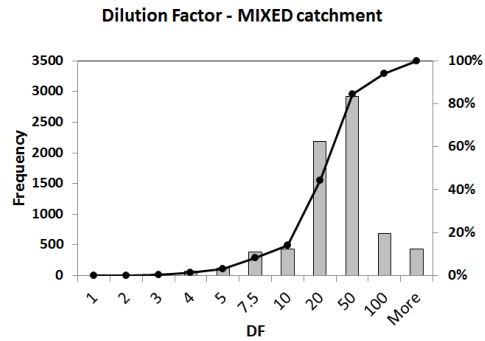
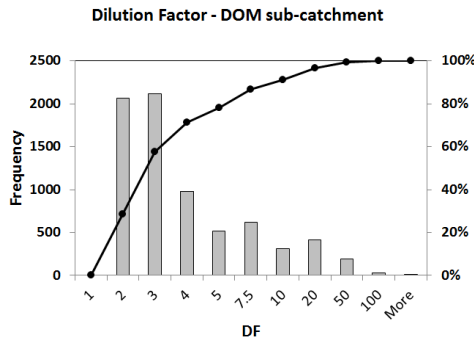
The effluent dilution factor of the domestic wastewater treatment plant in the (sub-)catchments varied with time, and ranged from 2 to >100 for the CITY scenario (P50 \cong 4),

and from 7.5 to >100 for the MIXED land use scenario ($P50 \cong 20$). As an example, the domestic discharge effluent dilution factor (DF) in the (sub-)catchment varies with time, linked to rainfall events and hydrological conditions. Domestic sub-catchment and mixed

catchment DF-variation are shown in

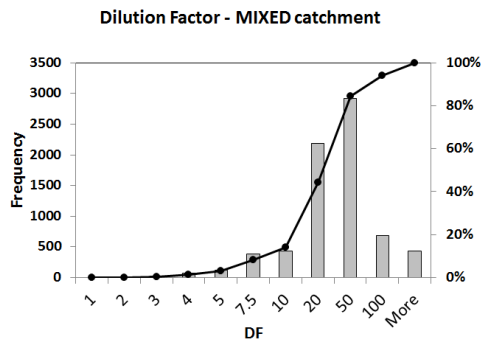
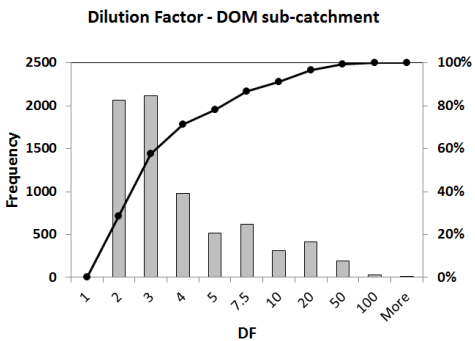


S.I. Figure 3.



INSERT

S.I. Figure 3 HERE



S.I. Figure 3. Variation in the dilution factor of effluents for two land use scenario layouts. Inflow of effluents from the DOM-scenario is $0.0231 \text{ m}^3/\text{sec}$.

Measured and Predicted Environmental Concentrations (MECs and PECs)

Measured and Predicted Environmental Concentrations (MECs and PECs) were collated from literature sources and the scenario modelling, respectively. MECs were obtained from the EMPODAT database, designed and managed by the NORMAN network (<http://www.norman-network.net/empodat/>; the NORMAN network is a European network of reference laboratories, research centers and related organizations for monitoring of emerging environmental substances). MECs were downloaded from EMPODAT on April 2, 2017, for all studied chemicals, by selecting “Water - Surface water – River water” as Ecosystems/Matrices query, and “Monitoring” as Type of Data Source query. Additionally MECs were obtained from the European Environment Agency Waterbase database (<http://www.eea.europa.eu/data-and-maps/data/waterbase-water-quality/>). MECs were downloaded from the Waterbase on March 31, 2017. Further MECs were obtained from other literature sources. Results are summarized in S.I. Table 5 for the chemicals studied in the AGR scenario, S.I. Table 6 for those in the DOM scenario, and S.I. Table 7 for those in the URB scenario. Note that the percentile values for EMPODAT data represent the percentiles for measured concentrations higher than the Level of Quantification (LOQ), and that – most often – measurements for a very large number of river water samples compound resulted in observed concentrations below the LOQ.

An illustration of the comparison of MECs and PECs (P95 value of the concentration at the outflow of a sub-catchment) has been made for sub-catchments with one land use (either AGR or CITY, which collates DOM and URB), and for the MIXED land use (outflow of whole catchment). Values marked grey in the MEC and PEC columns, respectively, indicate the MEC and PEC concentrations which are most closely related. For example, for the AGR scenario, a literature-based MEC of boscalid (measured in U.S. surface waters), tabulated as P50, is closely similar to the P95-PEC of the AGR sub-catchment as well as to the P95-PEC of the MIXED catchment outflow.

SCENARIOS AND CHEMICALS				MONITORING DATA SETS OR LITERATURE DATA										SCENARIO PECs		DATA SOURCES	
SCENARIO	CHEMICAL	ABBREV.	CAS. NO.	µg/L										(P95, µg/L)		Reference	
				#DATA	#DETECT	%DETECT	5th	25th	50th	75th	95th	99.9th	CITY or AGR	MIXED			
AGR	Boscalid	A-BOS	188425-85-6	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
AGR	Boscalid	A-BOS	188425-85-6	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
AGR	Boscalid	A-BOS	188425-85-6							0.026			0.109		0.022	0.042	Reilly et al., US study
AGR	Chlorothalonil	A-CHLOR	1897-45-6	48612	59	0.13%	0.002	0.009	0.020	0.054	0.175	14.234		5.2E-06	0.001		EMPODAT (1-4-2017)
AGR	Chlorothalonil	A-CHLOR	1897-45-6	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Chlorothalonil	A-CHLOR	1897-45-6							<DL		0.228					Reilly et al., US study
AGR	Cypermethrin	A-CYP	52315-07-8	30729	188	0.61%	0.001	0.002	0.002	0.003	0.016	0.378		0.001	0.0012		EMPODAT (1-4-2017)
AGR	Cypermethrin	A-CYP	52315-07-8	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Cypermethrin	A-CYP	52315-07-8														
AGR	Epoxiconazole	A-EPOX	133855-98-8	nd	nd	nd	nd	nd	nd	nd	nd	nd					EMPODAT (1-4-2017)
AGR	Epoxiconazole	A-EPOX	133855-98-8	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Epoxiconazole	A-EPOX	133855-98-8										0.028	0.035			
AGR	Flufenacet	A-FLUF	142459-58-3	20029	833	4.16%	0.009	0.012	0.021	0.037	0.130	4.034		0.0003	0.005		EMPODAT (1-4-2017)
AGR	Flufenacet	A-FLUF	142459-58-3	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Flufenacet	A-FLUF	142459-58-3														
AGR	Fluoxastrobin	A-FLUO	175013-18-0	nd	nd	nd	nd	nd	nd	nd	nd	nd					EMPODAT (1-4-2017)
AGR	Fluoxastrobin	A-FLUO	175013-18-0	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Fluoxastrobin	A-FLUO	175013-18-0										0.004	0.005			
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	nd	nd	nd	nd	nd	nd	nd	nd	nd					EMPODAT (1-4-2017)
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7										9.5E-08	3.2E-08			
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	nd	nd	nd	nd	nd	nd	nd	nd	nd					EMPODAT (1-4-2017)
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6										2.9E-06	7.6E-06			
AGR	Pendimethalin	A-PEND	40487-42-1	72389	807	1.11%	0.010	0.014	0.023	0.050	0.180	1.378		0.150	0.121		EMPODAT (1-4-2017)
AGR	Pendimethalin	A-PEND	40487-42-1	5388	nd	nd	0.005	nd	0.026	nd	0.100	nd					EEA-Waterbase (31-3-2017)
AGR	Pendimethalin	A-PEND	40487-42-1	nd	nd	nd	nd	nd	0.033	nd	0.057	nd					Reilly et al., US study
AGR	Prochloraz	A-PROCH	67747-09-5	36748	393	1.07%	0.0016	0.007	0.019	0.06	0.254	2.04344		0.030	0.021		EMPODAT (1-4-2017)
AGR	Prochloraz	A-PROCH	67747-09-5	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Prochloraz	A-PROCH	67747-09-5	nd	nd	nd	nd	nd	nd	nd	nd	nd					
AGR	Proquinazid	A-PROQ	189278-12-4	nd	nd	nd	nd	nd	nd	nd	nd	nd					EMPODAT (1-4-2017)
AGR	Proquinazid	A-PROQ	189278-12-4	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Proquinazid	A-PROQ	189278-12-4										0.0006	0.0005			
AGR	Prothioconazole	A-PROT	178928-70-6	nd	nd	nd	nd	nd	nd	nd	nd	nd					EMPODAT (1-4-2017)
AGR	Prothioconazole	A-PROT	178928-70-6	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Prothioconazole	A-PROT	178928-70-6	nd	nd	nd	nd	nd	nd	nd	nd	nd		3.6E-10	1.2E-10		
AGR	Pyraclastrobin	A-PYRA	175013-18-0	nd	nd	nd	nd	nd	nd	nd	nd	nd					EMPODAT (1-4-2017)
AGR	Pyraclastrobin	A-PYRA	175013-18-0	0	nd	nd	nd	nd	nd	nd	nd	nd					EEA-Waterbase (31-3-2017)
AGR	Pyraclastrobin	A-PYRA	175013-18-0	nd	nd	nd	nd	nd	0.0152	nd	0.239	nd		0.001	0.001		Reilly et al., US study

S.I. Table 5. Measured- and Predicted Environmental Concentrations of chemicals studied in the AGR scenario. Grey backgrounds indicate the closest similarity of PECs and MECs. Reilly et al. reference is: [14].

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SCENARIOS AND CHEMICALS				MONITORING DATA SETS OR LITERATURE DATA										SCENARIO PECs		DATA SOURCES	
SCENARIO	CHEMICAL	ABBREV.	CAS. NO.	µg/L										(µg/L)		Reference	
				#DATA	#DETECT	%DETECT	5th	25th	50th	75th	95th	99th	CITY or AGR	MIXED			
DOM	1-OH-Benzotriazole	D-BTZ	8001-54-5	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	1-OH-Benzotriazole	D-BTZ	8001-54-5	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	1-OH-Benzotriazole	D-BTZ	8001-54-5	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	11.271	4.927	
DOM	Acesulfame	D-ACS	55589-62-3	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	Acesulfame	D-ACS	55589-62-3	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Acesulfame	D-ACS	55589-62-3	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	41.141	17.983	
DOM	Benzalkonium chloride	D-BAC	53516-76-0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	Benzalkonium chloride	D-BAC	53516-76-0	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Benzalkonium chloride	D-BAC	53516-76-0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	0.061	0.027	
DOM	Caffeine	D-CAF	58-08-2	14598	12788	88%	0.019	0.063	0.13	0.26	0.77	6.3852	180.343	78.830			EMPODAT (1-4-2017)
DOM	Caffeine	D-CAF	58-08-2	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Caffeine	D-CAF	58-08-2	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			
DOM	Carbamazepin	D-CMZ	298-46-4	21299	16678	78%	0.022	0.045	0.0865	0.19	0.62	3.6	4.103	1.793			EMPODAT (1-4-2017)
DOM	Carbamazepin	D-CMZ	298-46-4	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Carbamazepin	D-CMZ	298-46-4	nd	nd	nd	0.058	nd	0.121	nd	nd	nd	nd	nd			Pomati et al.,(2017)
DOM	Erythromycin Sulfomethoxazole	D-SMX	723-46-6	2115	1496	71%	0.006	0.016	0.025	0.045	0.11	0.5507	7.890	3.449			EMPODAT (1-4-2017)
DOM	Erythromycin Sulfomethoxazole	D-SMX	723-46-6	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Erythromycin Sulfomethoxazole	D-SMX	723-46-6	nd	nd	nd	0.005	nd	0.007	nd	nd	nd	nd	nd			Pomati et al.,(2017)
DOM	Ethinylestradiol	D-EE2	57-63-6	1448	9	1%	0.01	0.02	0.021	0.04	0.08	0.08	0.001	0.0005			EMPODAT (1-4-2017)
DOM	Ethinylestradiol	D-EE2	57-63-6	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Ethinylestradiol	D-EE2	57-63-6	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			
DOM	HHCb (Galaxolide)	D-HHCB	1222-05-5	22612	11568	51%	0.013	0.025	0.044	0.081	0.23	1.2866	32.732	14.308			EMPODAT (1-4-2017)
DOM	HHCb (Galaxolide)	D-HHCB	1222-05-5	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	HHCb (Galaxolide)	D-HHCB	1222-05-5	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			
DOM	Ibuprofen	D-IBU	15687-27-1	4620	3238	70%	0.008	0.02	0.039	0.076	0.25	20.526	6.970	3.046			EMPODAT (1-4-2017)
DOM	Ibuprofen	D-IBU	15687-27-1	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Ibuprofen	D-IBU	15687-27-1	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			Pomati et al.,(2017)
DOM	Linear alkylbenzene sulphonate (C11.6)	D-LAS	68411-30-3	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	Linear alkylbenzene Sulphonate (C11.6)	D-LAS	68411-30-3	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Linear alkylbenzene sulphonate (C11.6)	D-LAS	68411-30-3	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	22.543	9.854	
DOM	Methylisothiazolinone	D-MI	2682-20-4	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	Methylisothiazolinone	D-MI	2682-20-4	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Methylisothiazolinone	D-MI	2682-20-4	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	1.127	0.493	
DOM	TiO	D-TiO	13463-67-7	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	TiO	D-TiO	13463-67-7	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	TiO	D-TiO	13463-67-7	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	10.990	4.804	
DOM	Zinc acetate	D-ZnA	557-34-6	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	Zinc acetate	D-ZnA	557-34-6	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	Zinc acetate	D-ZnA	557-34-6	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	3.115	1.362	
DOM	ZnO	D-ZnO	1314-13-2	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
DOM	ZnO	D-ZnO	1314-13-2	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
DOM	ZnO	D-ZnO	1314-13-2	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	63.496	27.755	

S.I. Table 6. Measured- and Predicted Environmental Concentrations of chemicals studied in the domestic scenario. Grey backgrounds indicate the closest similarity of PECs and MECs. Pomati et al reference is: [15].

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SCENARIOS AND CHEMICALS				MONITORING DATA SETS OR LITERATURE DATA									SCENARIO PECs		DATA SOURCES
SCENARIO	CHEMICAL	ABBREV.	CAS. NO.	#DATA	#DETECT	%DETECT	µg/L					999th	CITY or AGR	MIXED	Reference
							5th	25th	50th	75th	95th				
URB	Aluminum reactive	U-ALU	7429-90-5	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
URB	Aluminum reactive	U-ALU	7429-90-5	0	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
URB	Aluminum reactive	U-ALU	7429-90-5	nd	nd	nd	nd	nd	nd	nd	nd	nd	1.046	0.414	
URB	Benz(a)anthracene	U-BaA	56-55-3	55164	23108	0.418896	0.001	0.002	0.0041	0.0092	0.034	112.4	0.008	0.0033	EMPODAT (1-4-2017)
URB	Benz(a)anthracene	U-BaA	56-55-3	0	nd	nd	0.0005	nd	0.005	nd	0.01	nd			EEA-Waterbase (31-3-2017)
URB	Benz(a)anthracene	U-BaA	56-55-3	nd	nd	nd	nd	nd	nd	nd	nd	nd			
URB	Bifenthrin	U-BIF	82657-04-3	16691	1	nd	nd	nd	0.037	nd	nd	nd	0.0013	0.0005	EMPODAT (1-4-2017)
URB	Bifenthrin	U-BIF	82657-04-3	0	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
URB	Bifenthrin	U-BIF	82657-04-3	nd	nd	nd	nd	nd	nd	nd	nd	nd			
URB	Copper dissolved	U-CU	7440-50-8	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
URB	Copper dissolved	U-CU	7440-50-8	3763	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
URB	Copper dissolved	U-CU	7440-50-8	nd	nd	nd	nd	nd	nd	nd	nd	nd	1.427	0.564	
URB	Deltamethrin	U-DELTA	52918-63-5	48953	112	0.23%	0.00008	0.00014	0.00025	0.001425	0.08515	0.17112	0.0036	0.0014	EMPODAT (1-4-2017)
URB	Deltamethrin	U-DELTA	52918-63-5	0	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
URB	Deltamethrin	U-DELTA	52918-63-5	nd	nd	nd	nd	nd	nd	nd	nd	nd			
URB	Fluoranthene	U-FLUO	206-44-0	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
URB	Fluoranthene	U-FLUO	206-44-0	4463	nd	nd	0.0005	nd	0.005	nd	0.03	nd	0.038	0.015	EEA-Waterbase (31-3-2017)
URB	Fluoranthene	U-FLUO	206-44-0	nd	nd	nd	nd	nd	nd	nd	nd	nd			
URB	Iron dissolved	U-FE	7439-89-6	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
URB	Iron dissolved	U-FE	7439-89-6	159	nd	nd	50	nd	50	nd	99.7	nd	47.8	18.9	EEA-Waterbase (31-3-2017)
URB	Iron dissolved	U-FE	7439-89-6	nd	nd	nd	nd	nd	nd	nd	nd	nd			
URB	Nonylphenol ethoxylate	U-NP1EO	9016-45-9	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
URB	Nonylphenol ethoxylate	U-NP1EO	9016-45-9	0	nd	nd	nd	nd	nd	nd	nd	nd			EEA-Waterbase (31-3-2017)
URB	Nonylphenol ethoxylate	U-NP1EO	9016-45-9	nd	nd	nd	nd	nd	nd	nd	nd	nd	0.180	0.071	
URB	Permethrin	U-PER	52645-53-1	34895	17	0.049%	0.0214	0.04	0.092	0.15	0.568	0.75616	0.0087	0.0035	EMPODAT (1-4-2017)
URB	Permethrin	U-PER	52645-53-1	159	nd	nd	0.03	nd	0.03	nd	0.1	nd			EEA-Waterbase (31-3-2017)
URB	Permethrin	U-PER	52645-53-1	nd	nd	nd	nd	nd	nd	nd	nd	nd			
URB	Zinc dissolved	U-ZN	7440-66-6	nd	nd	nd	nd	nd	nd	nd	nd	nd			EMPODAT (1-4-2017)
URB	Zinc dissolved	U-ZN	7440-66-6	4072	nd	nd	3	nd	10	nd	30	nd			EEA-Waterbase (31-3-2017)
URB	Zinc dissolved	U-ZN	7440-66-6	nd	nd	nd	nd	nd	nd	nd	nd	nd	3.631	1.437	

S.I. Table 7. Measured- and Predicted Environmental Concentrations of chemicals studied in the urban scenario. Grey backgrounds indicate the closest similarity of PECs and MECs.

Predicted Environmental Concentrations (PECs) and effect endpoints

Effect endpoints were collated from the three scenario manuscripts, literature and databases. The summary data are presented in S.I. Tables 7, 8 and 9.

SCENARIOS AND CHEMICALS					P95 (SCENARIOS), CRITERIA & ECO-TEST DATA				APPLICATION FACTORS & REGULATORY					
SCENARIO	CHEMICAL	ABBREV.	CAS	PRIMARY-MOA	µg/L				ACCEPTABLE CONCENTRATIONS (PNECs or RACs) & REF (1)					
					DATA ENTRY	A/C	PODI (1/N)	CONC (µg/L)	AF	RACs (µg/L)	TAXA	REF (1)		
AGR	Boscalid	A-BOS	188425-85-6	pyridine	P95-AGR			0	0.022					
AGR	Boscalid	A-BOS	188425-85-6	pyridine	AA-EQS (indicative MTR, dissolved)			2	0.55			All	RIVM-RVS	
AGR	Boscalid	A-BOS	188425-85-6	pyridine	Chronic NOEC-HCS			4	15			All	SSD-RIVM	
AGR	Boscalid	A-BOS	188425-85-6	pyridine	Acute EC50-HCS0			5	2874			All	SSD-RIVM	
AGR	Boscalid	A-BOS	188425-85-6	pyridine	Primary producers		C	6	1340		10	134	Primary producers	Agriculture-MS
AGR	Boscalid	A-BOS	188425-85-6	pyridine	Invertebrates		C	8	1000		100	100	Invertebrates	Agriculture-MS
AGR	Boscalid	A-BOS	188425-85-6	pyridine	Invertebrates		A	9	5330		100	53.3	Invertebrates	Agriculture-MS
AGR	Boscalid	A-BOS	188425-85-6	pyridine	Fish		C	10	125		100	12.5	Fish	Agriculture-MS
AGR	Boscalid	A-BOS	188425-85-6	pyridine	Fish		A	11	2700		100	27	Fish	Agriculture-MS
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	P95-AGR			0	5.2E-06					
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	Chronic NOEC-HCS			4	0.45			All	SSD-RIVM	
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	Acute EC50-HCS0			5	103			All	SSD-RIVM	
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	Primary producers		C	6	30		3	10	Primary producers	Agriculture-MS
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	Invertebrates		A	7	84		100	0.84	Invertebrates	Agriculture-MS
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	Invertebrates		C	8	30		3	10	Invertebrates	Agriculture-MS
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	Fish		C	10	3		100	0.3	Fish	Agriculture-MS
AGR	Chlorothalonil	A-CHLOR	1897-45-6	aromatic	Fish		A	11	38		100	0.38	Fish	Agriculture-MS
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	P95-AGR			0	0.001					
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	AA-EQS (total)			2	0.00008					
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	MAC-EQS (total)			3	0.0006					
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	Chronic NOEC-HCS			4	0.009					SSD-RIVM
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	Acute EC50-HCS0			5	0.772			All	SSD-RIVM	
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	Primary producers		C	6	143000		10	14300	Primary producers	Agriculture-MS
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	Invertebrates		C	8	0.015		3	0.005	Invertebrates	Agriculture-MS
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	Invertebrates		A	9	0.0069		100	0.00069	Invertebrates	Agriculture-MS
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	Fish		C	10	0.077		100	0.0077	Fish	Agriculture-MS
AGR	Cypermethrin	A-CYP	52315-07-8	pyrethroid ester	Fish		A	11	2.66		100	0.027	Fish	Agriculture-MS
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	P95-AGR			0	0.028					
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	AA-EQS (dissolved)			2	0.190			All	RIVM-RVS	
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	MAC-EQS (dissolved)			3	1.800			All	RIVM-RVS	
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	Chronic NOEC-HCS			4	4.351			All	SSD-RIVM	
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	Acute EC50-HCS0			5	542			All	SSD-RIVM	
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	Primary producers (Lemna)		C	6	14		10	1.38	Primary producers	Agriculture-MS
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	Invertebrates		C	8	63		100	6.25	Invertebrates	Agriculture-MS
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	Invertebrates		A	9	8690		100	86.9	Invertebrates	Agriculture-MS
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	Fish		C	10	10		100	1	Fish	Agriculture-MS
AGR	Epoxiconazole	A-EPOX	133855-98-8	conazole	Fish		A	11	3140		100	31.4	Fish	Agriculture-MS
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	P95-AGR			0	3.3E-04					
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	AA-EQS (dissolved)			2	0.137			All	RIVM-RVS	
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	MAC-EQS (dissolved)			3	0.61			All	RIVM-RVS	
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	Chronic NOEC-HCS			4	6.228			All	SSD-RIVM	
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	Acute EC50-HCS0			5	3880			All	SSD-RIVM	
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	Primary producers		C	6	12		3	4	Primary producers	Agriculture-MS
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	Invertebrates		C	8	3260		10	326	Invertebrates	Agriculture-MS
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	Invertebrates		A	9	30900		100	309	Invertebrates	Agriculture-MS
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	Fish		C	10	200		100	20	Fish	Agriculture-MS
AGR	Flufenacet	A-FLUF	142459-58-3	anilide	Fish		A	11	2130		100	21.3	Fish	Agriculture-MS
AGR	Fluoxastrobin	A-FLUO	175013-18-0	175013-18-0	P95-AGR			0	0.004					
AGR	Fluoxastrobin	A-FLUO	175013-18-0	175013-18-0	AA-EQS (dissolved)			2	0.012			All	RIVM-RVS	
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	MAC-EQS (dissolved)			3	0.64			All	RIVM-RVS	
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	Chronic NOEC-HCS			4	11.8			All	SSD-RIVM	
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	Acute EC50-HCS0			5	700			All	SSD-RIVM	
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	Primary producers		C	6	350		10	35	Primary producers	Agriculture-MS
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	Invertebrates		C	8	180		10	180	Invertebrates	Agriculture-MS
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	Invertebrates		A	9	480		100	4.8	Invertebrates	Agriculture-MS
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	Fish		C	10	28.6		100	2.86	Fish	Agriculture-MS
AGR	Fluoxastrobin	A-FLUO	361377-29-9	361377-29-9	Fish		A	11	435		100	4.35	Fish	Agriculture-MS
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	P95-AGR			0	9.5E-08					
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	Chronic NOEC-HCS			4	42			All	SSD-RIVM	
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	Acute EC50-HCS0			5	26170			All	SSD-RIVM	
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	Primary producers		C	6	70		10	7	Primary producers	Agriculture-MS
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	Invertebrates		C	8	10000		100	1000	Invertebrates	Agriculture-MS
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	Invertebrates		A	9	>100000		100	>1000	Invertebrates	Agriculture-MS
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	Fish		C	10	10000		100	1000	Fish	Agriculture-MS
AGR	Iodosulfuron-methyl	A-IODO	144550-36-7	144550-36-7	Fish		A	11	>100000		100	>1000	Fish	Agriculture-MS
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	P95-AGR			0	2.89143E-06					
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	AA-EQS (dissolved)			2	0.01			All	RIVM-RVS	
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	MAC-EQS (dissolved)			3	0.03			All	RIVM-RVS	
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	Chronic NOEC-HCS			4	15.535			All	SSD-RIVM	
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	Acute EC50-HCS0			5	4413			All	SSD-RIVM	
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	Primary producers		C	6	113.4		10	11.34	Primary producers	Agriculture-MS
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	Invertebrates		C	8	3130		100	313	Invertebrates	Agriculture-MS
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	Invertebrates		A	9	43100		100	431	Invertebrates	Agriculture-MS
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	Fish		C	10	68000		100	6800	Fish	Agriculture-MS
AGR	Mesosulfuron-methyl	A-MESO	74223-64-6	PLANT GROWTH REGULATOR	Fish		A	11	>113000		100	>1130	Fish	Agriculture-MS

AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	P95-AGR	0	0.150					
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	AA-EQS (dissolved)	2	0.018				All	RIVM-RV
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	MAC-EQS (dissolved)	3	0.024				All	RIVM-RV
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	Chronic NOEC-HC5	4	1.639				All	SSD-RIV
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	Acute EC50-HC50	5	951.5				All	SSD-RIV
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	Primary producers	C	6	1.1	1		1.1 Primary producers	Agriculture
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	Invertebrates	C	8	14.5	10		1.45 Invertebrates	Agriculture
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	Invertebrates	A	9	280	100		2.8 Invertebrates	Agriculture
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	Fish	C	10	6	10		0.6 Fish	Agriculture
AGR	Pendimethalin	A-PEND	40487-42-1	dinitroaniline	Fish	A	11	138	100		1.38 Fish	Agriculture
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	P95-AGR	0	0.030					
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	AA-EQS (indicative MTR, dissolved)	2	1.3				All	RIVM-RV
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	Chronic NOEC-HC5	4	8.08				All	SSD-RIV
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	Acute EC50-HC50	5	1006.0				All	SSD-RIV
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	Primary producers	C	6	> 32	10		> 3,2 Primary producers	Agriculture
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	Invertebrates	C	8	22.2	10		2.22 Invertebrates	Agriculture
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	Invertebrates	A	9	770	100		7.7 Invertebrates	Agriculture
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	Fish	C	10	24.9	10		2.49 Fish	Agriculture
AGR	Prochloraz	A-PROCH	67747-09-5	conazole	Fish	A	11	1200	100		12 Fish	Agriculture
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	P95-AGR	0	0.001					
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Chronic NOEC-HC5 (extrapol.)	4	0.706				All	RIVM-RV
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Acute EC50-HC50	5	100.0				All	SSD-RIV
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Primary producers	C	6	250	10		25 Primary producers	Agriculture
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Invertebrate chronic (RAC)	7	0.180				All	RIVM-RV
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Invertebrates	C	8	1.8	10		0.18 Invertebrates	Agriculture
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Invertebrates	A	9	287	100		2.87 Invertebrates	Agriculture
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Fish	C	10	3	10		0.3 Fish	Agriculture
AGR	Proquinazid	A-PROQ	189278-12-4	fungicide	Fish	A	11	349	100		3.49 Fish	Agriculture
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	P95-AGR	0	3.6E-10					
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	AA-EQS (dissolved)	2	3.700				All	RIVM-RV
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	Chronic NOEC-HC5	4	13.238				All	SSD-RIV
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	Acute EC50-HC50	5	1436.8				All	SSD-RIV
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	Primary producers	C	6	2180.0	10		218 Primary producers	Agriculture
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	Invertebrates	C	8	560.0	10		56 Invertebrates	Agriculture
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	Invertebrates	A	9	1300.0	100		13 Invertebrates	Agriculture
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	Fish	C	10	308.0	10		30.8 Fish	Agriculture
AGR	Prothioconazole	A-PROT	178928-70-6	conazole	Fish	A	11	1830.0	100		18.3 Fish	Agriculture
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	P95-AGR	0	0.001					
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	AA-EQS (indicative MTR, dissolved)	2	0.023				All	RIVM-RV
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	Chronic NOEC-HC5	4	0.943				All	SSD-RIV
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	Acute EC50-HC50	5	20.711				All	SSD-RIV
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	Primary producers	C	6	>843	10		>84.3 Primary producers	Agriculture
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	Invertebrates	C	8	4	10		0.4 Invertebrates	Agriculture
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	Invertebrates	A	9	16	100		0.16 Invertebrates	Agriculture
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	Fish	C	10	2	10		0.2 Fish	Agriculture
AGR	Pyraclostrobin	A-PYRA	175013-18-0	strobin	Fish	A	11	6	100		0.06 Fish	Agriculture

S.I. Table 8. Predicted Environmental Concentrations (P95-values at the outlet of an AGR-sub-catchment) compared with various regulatory criteria and test endpoints. Block “Scenarios and chemicals”: the chemicals, their abbreviations, their CAS-numbers, and their assigned mode of action. Block “P95 (Scenarios), Criteria & eco-test data”: the measured P95 (in grey), Acute or Chronic test endpoints (A/C), a PODI-code (Point of Departure Index, coding the different benchmarks), and the criterion or test concentration (in µg/L). Situations in which the P95-PEC at the outlet of a (sub-)catchment is higher than the regulatory criterion or test endpoint are marked with a bold outline.

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SCENARIOS AND CHEMICALS					P95 (SCENARIOS), CRITERIA & ECO-TEST DATA			SCENARIOS AND CHEMICALS		
					µg/L					
DOM	1-OH-Benzotriazole (BTZ)	D-BTZ	8001-54-5	chloride unclassified	P95_DOMESTIC	0	11.271			
DOM	1-OH-Benzotriazole (BTZ)	D-BTZ	8001-54-5	chloride unclassified	PNEC	C	1		50	100
DOM	1-OH-Benzotriazole (BTZ)	D-BTZ	8001-54-5	chloride unclassified	Chronic NOEC-HCS		4.478		All	
DOM	1-OH-Benzotriazole (BTZ)	D-BTZ	8001-54-5	chloride unclassified	Acute EC50-HCS0		759		All	
DOM	1-OH-Benzotriazole (BTZ)	D-BTZ	8001-54-5	chloride unclassified	Primary producers	C	6	10000	Primary producers	
DOM	1-OH-Benzotriazole (BTZ)	D-BTZ	8001-54-5	chloride unclassified	Invertebrates	C	8	1580	Invertebrates	
DOM	1-OH-Benzotriazole (BTZ)	D-BTZ	8001-54-5	chloride unclassified	Fish	C	10	18000	Fish	
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	P95_DOMESTIC	0	41.141			
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	PNEC	C	1		1	1000
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	About PODI=AllTaxa&ExtrapChronicNOEC-HCS		7057		All	
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	Acute EC50-HCS0		1000000		All	
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	Primary producers	C	6	>100000	Primary producers	
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	Invertebrates	C	8	>100000	Invertebrates	
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	Fish	C	10	1000	Fish	
DOM	Acetulfame	D-ACS	55589-62-3	55589-62-3	AllTaxa&ExtrapChronicNOEC-HCS0					
DOM	Benzalkonium chloride (BAC)	D-BAC	53516-76-0	53516-76-0	P95_DOMESTIC	0	0.061			
DOM	Benzalkonium chloride (BAC)	D-BAC	53516-76-0	53516-76-0	PNEC	C	1		10	1.14
DOM	Benzalkonium chloride (BAC)	D-BAC	53516-76-0	53516-76-0	Chronic NOEC-HCS		10.605			
DOM	Benzalkonium chloride (BAC)	D-BAC	53516-76-0	53516-76-0	Acute EC50-HCS0		1760		All	
DOM	Benzalkonium chloride (BAC)	D-BAC	53516-76-0	53516-76-0	Primary producers	C	6		Primary producers	
DOM	Benzalkonium chloride (BAC)	D-BAC	53516-76-0	53516-76-0	Invertebrates	C	8	11.4	Invertebrates	
DOM	Benzalkonium chloride (BAC)	D-BAC	53516-76-0	53516-76-0	Fish	C	10	170	Fish	
DOM	Caffeine	D-CAF	58-08-2	pyridine	P95_DOMESTIC	0	180.343			
DOM	Caffeine	D-CAF	58-08-2	pyridine	PNEC	C	1		1000	87
DOM	Caffeine	D-CAF	58-08-2	pyridine	Chronic NOEC-HCS		4,000	70	RIVM/	
DOM	Caffeine	D-CAF	58-08-2	pyridine	Acute EC50-HCS0		16539		All	
DOM	Caffeine	D-CAF	58-08-2	pyridine	Primary producers	C	6	6250	Primary producers	
DOM	Caffeine	D-CAF	58-08-2	pyridine	Invertebrates	C	8	18200	Invertebrates	
DOM	Caffeine	D-CAF	58-08-2	pyridine	Fish	C	10	8700	Fish	
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	P95_DOMESTIC	0	4.103			
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	PNEC	C	1		10	2.5
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	AA-EQS (dissolved)		0.500		All	
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	MAC-EQS (dissolved)		1600		RIVM/	
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	Chronic NOEC-HCS		3.473		All	
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	Acute EC50-HCS0		38744		All	
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	Primary producers	C	6	>100000	Primary producers	
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	Invertebrates	C	8	25	Invertebrates	
DOM	Carbamazepin	D-CMZ	298-46-4	Antiepileptics(n=4)	Fish	C	10	25000	Fish	
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	P95_DOMESTIC	0	0.001			
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	PNEC	C	1		1	0.0003
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	AA-EQS (total)		0.000016		All	
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	MAC-EQS (total)		0.000560		All	
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	Chronic NOEC-HCS		0.000363		All	
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	Acute EC50-HCS0		1906		All	
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	Primary producers	C	6	0.00E+00	Primary producers	
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	Invertebrates	C	8	500	Invertebrates	
DOM	Ethinylestradiol	D-EE2	57-63-6	Estrogenic	Fish	C	10	0.000300	Fish	
DOM	HHCB (Galaxolide)	D-HHCB	1222-05-5	1222-05-5	P95_DOMESTIC	0	32.732			
DOM	HHCB (Galaxolide)	D-HHCB	1222-05-5	1222-05-5	PNEC	C	1		10	4.4
DOM	HHCB (Galaxolide)	D-HHCB	1222-05-5	1222-05-5	Chronic NOEC-HCS		7.057		All	
DOM	HHCB (Galaxolide)	D-HHCB	1222-05-5	1222-05-5	Acute EC50-HCS0		1000		All	
DOM	HHCB (Galaxolide)	D-HHCB	1222-05-5	1222-05-5	Primary producers	C	6	201	Primary producers	
DOM	HHCB (Galaxolide)	D-HHCB	1222-05-5	1222-05-5	Invertebrates	C	8	44	Invertebrates	
DOM	HHCB (Galaxolide)	D-HHCB	1222-05-5	1222-05-5	Fish	C	10	68	Fish	
DOM	Ibuprofen	D-IBU	15687-27-1	Analgesics, Anti-inflammatory Drugs and Antipyretics(n=4)	P95_DOMESTIC	0	6.970			
DOM	Ibuprofen	D-IBU	15687-27-1	Analgesics, Anti-inflammatory Drugs and Antipyretics(n=4)	PNEC	C	1		1000	7100
DOM	Ibuprofen	D-IBU	15687-27-1	Analgesics, Anti-inflammatory Drugs and Antipyretics(n=4)	Chronic NOEC-HCS		1.244		All	
DOM	Ibuprofen	D-IBU	15687-27-1	Analgesics, Anti-inflammatory Drugs and Antipyretics(n=4)	Acute EC50-HCS0		20305		All	
DOM	Ibuprofen	D-IBU	15687-27-1	Analgesics, Anti-inflammatory Drugs and Antipyretics(n=4)	Primary producers	C	6	34000	Primary producers	
DOM	Ibuprofen	D-IBU	15687-27-1	Analgesics, Anti-inflammatory Drugs and Antipyretics(n=4)	Invertebrates	C	8	14000	Invertebrates	
DOM	Ibuprofen	D-IBU	15687-27-1	Analgesics, Anti-inflammatory Drugs and Antipyretics(n=4)	Fish	C	10	25000	Fish	
DOM	Linear alkylbenzene sulphona	D-LAS	68411-30-3	non polar narcosis	P95_DOMESTIC	0	22.543			
DOM	Linear alkylbenzene sulphona	D-LAS	68411-30-3	non polar narcosis	PNEC	C	1		1	270
DOM	Linear alkylbenzene sulphona	D-LAS	68411-30-3	non polar narcosis	Acute EC50-HCS0		3225		All	
DOM	Linear alkylbenzene sulphona	D-LAS	68411-30-3	non polar narcosis	Primary producers	C	6	2400	Primary producers	
DOM	Linear alkylbenzene sulphona	D-LAS	68411-30-3	non polar narcosis	Invertebrates	C	8	290	Invertebrates	
DOM	Linear alkylbenzene sulphona	D-LAS	68411-30-3	non polar narcosis	Fish	C	10	270	Fish	
DOM	Methylisothiazolinone	D-MI	2682-20-4	non polar narcosis	P95_DOMESTIC	0	1.127			
DOM	Methylisothiazolinone	D-MI	2682-20-4	2682-20-4	PNEC	C	1		1	10
DOM	Methylisothiazolinone	D-MI	2682-20-4	2682-20-4	AA-EQS (indicative MTR, dissolved)		0.006		All	
DOM	Methylisothiazolinone	D-MI	2682-20-4	2682-20-4	Chronic NOEC-HCS		7.541		All	
DOM	Methylisothiazolinone	D-MI	2682-20-4	2682-20-4	Acute EC50-HCS0		189		All	
DOM	Methylisothiazolinone	D-MI	2682-20-4	2682-20-4	Primary producers	C	6	30	Primary producers	
DOM	Methylisothiazolinone	D-MI	2682-20-4	2682-20-4	Invertebrates	C	8	93	Invertebrates	
DOM	Methylisothiazolinone	D-MI	2682-20-4	2682-20-4	Fish	C	10	477	Fish	
DOM	Sulfamethoxazol	D-SMX	723-46-6	bactericides	P95_DOMESTIC	0	7.890			
DOM	Sulfamethoxazol	D-SMX	723-46-6	bactericides	PNEC	C	1		1	1.8
DOM	Sulfamethoxazol	D-SMX	723-46-6	bactericides	Chronic NOEC-HCS		9.858		All	
DOM	Sulfamethoxazol	D-SMX	723-46-6	bactericides	Acute EC50-HCS0		9445		All	
DOM	Sulfamethoxazol	D-SMX	723-46-6	bactericides	Primary producers	C	6	90000	Primary producers	
DOM	Sulfamethoxazol	D-SMX	723-46-6	bactericides	Invertebrates	C	8	8000	Invertebrates	
DOM	Sulfamethoxazol	D-SMX	723-46-6	bactericides	Fish	C	10	800000	Fish	
DOM	Titanium oxide (TiO2)	D-TiO	13463-67-7	Titanium	P95_DOMESTIC	0	10.990			
DOM	Titanium oxide (TiO2)	D-TiO	13463-67-7	Titanium	PNEC	C	1		1	184
DOM	Titanium oxide (TiO2)	D-TiO	13463-67-7	Titanium	Chronic NOEC-HCS		63		All	
DOM	Titanium oxide (TiO2)	D-TiO	13463-67-7	Titanium	Acute EC50-HCS0		18535		All	
DOM	Titanium oxide (TiO2)	D-TiO	13463-67-7	Titanium	Primary producers	C	6		Primary producers	
DOM	Titanium oxide (TiO2)	D-TiO	13463-67-7	Titanium	Invertebrates	C	8	18.4	Invertebrates	
DOM	Titanium oxide (TiO2)	D-TiO	13463-67-7	Titanium	Fish	C	10	29000	Fish	
DOM	Zinc acetate	D-ZNA	557-34-6	557-34-6	P95_DOMESTIC	0	3.115			
DOM	Zinc acetate	D-ZNA	557-34-6	557-34-6	PNEC	C	1		1	7.8
DOM	Zinc acetate	D-ZNA	557-34-6	557-34-6	Chronic NOEC-HCS		10		All	
DOM	Zinc acetate	D-ZNA	557-34-6	557-34-6	Acute EC50-HCS0		1628		All	
DOM	Zinc acetate	D-ZNA	557-34-6	557-34-6	Primary producers	C	6	7.8	Primary producers	
DOM	Zinc acetate	D-ZNA	557-34-6	557-34-6	Invertebrates	C	8	280	Invertebrates	
DOM	Zinc acetate	D-ZNA	557-34-6	557-34-6	Fish	C	10	2100	Fish	
DOM	Zinc oxide	D-ZNO	1314-13-2	Zinc	P95_DOMESTIC	0	63.496			
DOM	Zinc oxide	D-ZNO	1314-13-2	Zinc	PNEC	C	1			20.6
DOM	Zinc oxide	D-ZNO	1314-13-2	Zinc	Chronic NOEC-HCS		26		All	
DOM	Zinc oxide	D-ZNO	1314-13-2	Zinc	Acute EC50-HCS0		8568		All	
DOM	Zinc oxide	D-ZNO	1314-13-2	Zinc	Primary producers	C	6	17	Primary producers	
DOM	Zinc oxide	D-ZNO	1314-13-2	Zinc	Invertebrates	C	8	206	Invertebrates	
DOM	Zinc oxide	D-ZNO	1314-13-2	Zinc	Fish	C	10	10000	Fish	

S.I. Table 9. Predicted Environmental Concentrations (P95-values at the outlet of a CITY sub-catchment, for chemicals from the DOM-scenario) compared with various regulatory criteria and test endpoints. Block “Scenarios and chemicals”: the chemicals, their abbreviations, their CAS-numbers, and their assigned mode of action. Block “P95 (Scenarios), Criteria & eco-test data”: the measured P95 (in grey), Acute or Chronic test endpoints (A/C), a PODI-code (Point of Departure Index, coding the different benchmarks), and the criterion or test concentration (in µg/L). Situations in which the P95-PEC at the outlet of a (sub-)catchment is higher than the regulatory criterion or test endpoint are marked with a bold outline.

SCENARIOS AND CHEMICALS			P95 (SCENARIOS), CRITERIA & ECO-TEST DATA µg/L		SCENARIOS AND CHEMICALS		
U-ALU	7429-90-5	Aluminium	P95_URB	0	1.046		
U-ALU	7429-90-5	Aluminium	Chronic NOEC-HC5	4	14.6	All	SSD-RIVM
U-ALU	7429-90-5	Aluminium	Acute EC50-HC50	5	2242.3	All	SSD-RIVM
U-ALU	7429-90-5	Aluminium	Acute EC50-HC50	5	1925.0	All	Urban-M
U-BaA	56-55-3	non polar narcosis	P95_URB	0	0.008		
U-BaA	56-55-3	non polar narcosis	AA-EQS (total)	2	0.006	All	RIVM-RV
U-BaA	56-55-3	non polar narcosis	MAC-EQS (total)	3	0.280	All	RIVM-RV
U-BaA	56-55-3	non polar narcosis	Chronic NOEC-HC5	4	0.081	All	SSD-RIVM
U-BaA	56-55-3	non polar narcosis	Acute EC50-HC50	5	9.665	All	SSD-RIVM
U-BaA	56-55-3	non polar narcosis	Acute EC50-HC50	5	10.000	All	Urban-M
U-BIF	82657-04-3	pyrethroid ester	P95_URB	0	0.001		
U-BIF	82657-04-3	pyrethroid ester	AA-EQS (MTR, dissolved)	2	0.00010	All	RIVM-RV
U-BIF	82657-04-3	pyrethroid ester	Chronic NOEC-HC5	4	0.00091	All	SSD-RIVM
U-BIF	82657-04-3	pyrethroid ester	Acute EC50-HC50	5	1.043	All	SSD-RIVM
U-BIF	82657-04-3	pyrethroid ester	Acute EC50-HC50	5	1.000	All	Urban-M
U-CU	7440-50-8	copper	P95_URB	0	1.427		
U-CU	7440-50-8	copper	AA-EQS (dissolved)	2	2.400	All	RIVM/RV
U-CU	7440-50-8	copper	Chronic NOEC-HC5	4	0.501	All	SSD-RIVM
U-CU	7440-50-8	copper	Acute EC50-HC50	5	184	All	SSD-RIVM
U-CU	7440-50-8	copper	Acute EC50-HC50	5	183	All	Urban-M
U-DELTA	52918-63-5	pyrethroid ester	P95_URB	0	0.004		
U-DELTA	52918-63-5	pyrethroid ester	AA-EQS (dissolved)	2	0.000031		RIVM-RV
U-DELTA	52918-63-5	pyrethroid ester	MAC-EQS (dissolved)	3	0.00031		RIVM-RV
U-DELTA	52918-63-5	pyrethroid ester	Chronic NOEC-HC5	4	0.002		SSD-RIVM
U-DELTA	52918-63-5	pyrethroid ester	Acute EC50-HC50	5	1.967	All	SSD-RIVM
U-DELTA	52918-63-5	pyrethroid ester	Acute EC50-HC50	5	2.000	All	Urban-M
U-FLUO	206-44-0	non polar narcosis	P95_URB	0	0.038		
U-FLUO	206-44-0	non polar narcosis	AA-EQS (total)	2	0.006	All	RIVM-RV
U-FLUO	206-44-0	non polar narcosis	MAC-EQS (total)	3	0.120	All	RIVM-RV
U-FLUO	206-44-0	non polar narcosis	Chronic NOEC-HC5	4	0.972	All	SSD-RIVM
U-FLUO	206-44-0	non polar narcosis	Acute EC50-HC50	5	136	All	SSD-RIVM
U-FLUO	206-44-0	non polar narcosis	Acute EC50-HC50	5	136	All	Urban-M
U-FE	7439-89-6	Iron	P95_URB	0	47.813		
U-FE	7439-89-6	Iron	Chronic NOEC-HC5	4	199	All	SSD-RIVM
U-FE	7439-89-6	Iron	Acute EC50-HC50	5	25235	All	SSD-RIVM
U-FE	7439-89-6	Iron	Acute EC50-HC50	5	66298	All	Urban-M
U-NP1EO	9016-45-9	9016-45-9	P95_URB	0	0.180		
U-NP1EO	9016-45-9	9016-45-9	AA-EQS (MTR, dissolved)	2	0.110	All	RIVM/RV
U-NP1EO	9016-45-9	9016-45-9	Chronic NOEC-HC5	4	54	All	SSD-RIVM
U-NP1EO	9016-45-9	9016-45-9	Acute EC50-HC50	5	7354	All	SSD-RIVM
U-NP1EO	9016-45-9	9016-45-9	Acute EC50-HC50	5	525	All	Urban-M
U-PER	52645-53-1	pyrethroid ester	P95_URB	0	0.009		
U-PER	52645-53-1	pyrethroid ester	AA-EQS (MTR, dissolved)	2	0.00020	All	RIVM-RV
U-PER	52645-53-1	pyrethroid ester	Chronic NOEC-HC5	4	0.012	All	SSD-RIVM
U-PER	52645-53-1	pyrethroid ester	Acute EC50-HC50	5	12.12	All	SSD-RIVM
U-PER	52645-53-1	pyrethroid ester	Acute EC50-HC50	5	12.00	All	Urban-M
U-ZN	7440-66-6	Zinc	P95_URB	0	3.631		
U-ZN	7440-66-6	Zinc	AA-EQS (dissolved)	2	7.8	All	RIVM/RV
U-ZN	7440-66-6	Zinc	MAC-EQS (dissolved)	3	15.6	All	RIVM/RV
U-ZN	7440-66-6	Zinc	Chronic NOEC-HC5	4	5.7	All	SSD-RIVM
U-ZN	7440-66-6	Zinc	Acute EC50-HC50	5	1853	All	SSD-RIVM
U-ZN	7440-66-6	Zinc	Acute EC50-HC50	5	1903	All	Urban-M

S.I. Table 10. Predicted Environmental Concentrations (P95-values at the outlet of a CITY sub-catchment, for chemicals from the URB-scenario) compared with various regulatory criteria and test endpoints. Block “Scenarios and chemicals”: the chemicals, their abbreviations, their CAS-numbers, and their assigned mode of action. Block “P95 (Scenarios), Criteria & eco-test data”: the measured P95 (in grey), Acute or Chronic test endpoints (A/C), a PODI-code (Point of Departure Index, coding the different benchmarks), and the criterion or test concentration (in µg/L). Situations in which the P95-

PEC at the outlet of a (sub-)catchment is higher than the regulatory criterion or test endpoint are marked with a bold outline.

RESULTS: PRIORITIZATIONS

A prioritization of sample predictions regarding aspects of exposure time is summarized in S.I. Table 11.

SCENARIO	Metric, judgment SSD-NOEC-HC5	Total
1_Agriculture	Total number of days modeled	7246
	Maximum Σ RQ (or RQ)	9
	Number of days RQ > 1	191
	Num days Σ RQ > 1, but no single RQ > 1	81
	Number of days more than one RQ > 1	18
	Number of times consecutive days (Σ RQ > 1) is > 1	28
	Number of times consecutive days (Σ RQ > 1) is > 2	3
	Number of times consecutive days (Σ RQ > 1) is > 3	0
	Number of times consecutive days (Σ RQ > 1) is > 4	0
	2_City (Urban+Domestic)Urban	Total number of days modeled
Maximum Σ RQ (or RQ)		2310
Number of days RQ > 1		7194
Num days Σ RQ > 1, but no single RQ > 1		617
Number of days more than one RQ > 1		6352
Number of times consecutive days (Σ RQ > 1) is > 1		7164
Number of times consecutive days (Σ RQ > 1) is > 2		7134
Number of times consecutive days (Σ RQ > 1) is > 3		7105
Number of times consecutive days (Σ RQ > 1) is > 4		7077
3_CITY_NATURE		Total number of days modeled
	Maximum Σ RQ (or RQ)	1660
	Number of days RQ > 1	7108
	Num days Σ RQ > 1, but no single RQ > 1	1478
	Number of days more than one RQ > 1	5012
	Number of times consecutive days (Σ RQ > 1) is > 1	7032
	Number of times consecutive days (Σ RQ > 1) is > 2	6976
	Number of times consecutive days (Σ RQ > 1) is > 3	6925
	Number of times consecutive days (Σ RQ > 1) is > 4	6875
	3_Mixed	Total number of days modeled
Maximum Σ RQ (or RQ)		943
Number of days RQ > 1		6711
Num days Σ RQ > 1, but no single RQ > 1		4269
Number of days more than one RQ > 1		1918
Number of times consecutive days (Σ RQ > 1) is > 1		6553
Number of times consecutive days (Σ RQ > 1) is > 2		6432
Number of times consecutive days (Σ RQ > 1) is > 3		6316
Number of times consecutive days (Σ RQ > 1) is > 4		6206

S.I. Table 11. Prioritization information regarding maximum HI and exposure time variables.

A prioritization of the relative role of chemicals in the scenarios is summarized in S.I. Table 12. In the two sub-tables that are shown, a prioritization is made for the AGR-scenario chemicals. The evaluation is made for (left) exceedances of the regulatory AA-EQS (or the comparable type concentration value used for this) and (right) for the exceedance of the 95th-protection level. In the regulatory evaluation, the maximum HI_{AA-EQS} was 450 for one of the modelled days, and a number of 714 days for which the mixture hazard index exceeded 1. Cypermethrin was contributing most to the AA-EQS hazard indices (79%), followed by pendimethalin (17%). The next most important compounds regarding relative contributions to the HI are mesosulfuron-methyl, flufenacet and fluoxastrobin, etc. The prioritization for the aspect of time shows a different ranking. For example, an exceedance of the HQ for fluoxastrobin (using the AA-EQS as criterion) was predicted for 34% of the days at which the HI exceeded 1.

In the other table (right), the ranking towards magnitude and number of days is made using the 95th protection criterion (SSD-NOEC-HC5) as criterion to define the concentration above which direct chronic ecotoxicological effects are expected. The values for the maximum mixture HI and

the number of days for which the mixture HI>1 are much lower, relating to the multiple endpoints targeted for protection via the AA-EQS and the application factors, relating to uncertainties, in the AA-EQS assessment. Not only the magnitude of peak exceedances and numbers of days of exceedances is lowered, but also the rank order of chemicals contributing to these exceedances changed. This table ranks chlorothalonil high in its contribution to the maximum HI, and cypermethrin as compound ranking high in its relative number of days contributing to mixtures exceedances >1.

PRIORITIZATION OF CHEMICALS IN SCENARIOS

(a) WITH DIFFERENT DEFINITIONS OF THE HAZARD INDEX (BASED ON THE REGULATORY AA-EQS or SSD-NOEC-HC5)

(b) WITH DIFFERENT FOCUS (LEVEL OF EXCEEDANCES, left, AND DAYS WITH EXCEEDANCES, right)

Scenario	Metric	Chem-abbrev.	HI-Criterion	Max (Σ)HI	Day (Σ)HI > 1
AGR	ZRQs	Mixture	AA-EQS	450	714
AGR	Cypermethrin	A-CYP	AA-EQS	79%	73%
AGR	Pendimethalin	A-PEND	AA-EQS	17%	74%
AGR	Mesosulfuron-methyl	A-MESO	AA-EQS	8%	5%
AGR	Flufenacet	A-FLUF	AA-EQS	7%	13%
AGR	Fluoxastrobin	A-FLUO	AA-EQS	4%	34%
AGR	Chlorothalonil	A-CHLOR	AA-EQS	1%	4%
AGR	Epoxiconazole	A-EPOX	AA-EQS	1%	19%
AGR	Boscalid	A-BOS	AA-EQS	1%	8%
AGR	Pyraclostrobin	A-PYRA	AA-EQS	0%	0%
AGR	Prochloraz	A-PROCH	AA-EQS	0%	0%
AGR	Proquinazid	A-PROQ	AA-EQS	0%	0%
AGR	Prothioconazole	A-PROT	AA-EQS	0%	0%
AGR	Iodosulfuron-methyl	A-IODO	AA-EQS	0%	0%

Metric	Chem-abbrev.	HI-Criterion
ZRQs	Mixture	SSD-NOE
Chlorothalonil	A-CHLOR	SSD-NOE
Cypermethrin	A-CYP	SSD-NOE
Pendimethalin	A-PEND	SSD-NOE
Flufenacet	A-FLUF	SSD-NOE
Epoxiconazole	A-EPOX	SSD-NOE
Boscalid	A-BOS	SSD-NOE
Prochloraz	A-PROCH	SSD-NOE
Pyraclostrobin	A-PYRA	SSD-NOE
Mesosulfuron-methyl	A-MESO	SSD-NOE
Proquinazid	A-PROQ	SSD-NOE
Fluoxastrobin	A-FLUO	SSD-NOE
Prothioconazole	A-PROT	SSD-NOE
Iodosulfuron-methyl	A-IODO	SSD-NOE

Scenario	Metric	Chem-abbrev.	HI-Criterion	Max (Σ)HI	Day (Σ)HI > 1
CITY (URB + DOM)	ZRQs	Mixture	AA-EQS	472572	7191
CITY (URB + DOM)	Deltamethrin	U-DELTA	AA-EQS	72%	5%
CITY (URB + DOM)	Iron (dissolved)	U-FE	AA-EQS	24%	5%
CITY (URB + DOM)	Permethrin	U-PER	AA-EQS	3%	5%
CITY (URB + DOM)	Bifenthrin	U-BIF	AA-EQS	1%	5%
CITY (URB + DOM)	Fluoranthene	U-FLUO	AA-EQS	0%	5%
CITY (URB + DOM)	Nonylphenol ethoxylate	U-NP1EO	AA-EQS	0%	5%
CITY (URB + DOM)	Benz(a)anthracene	U-BaA	AA-EQS	0%	5%
CITY (URB + DOM)	Copper (dissolved)	U-CU	AA-EQS	0%	5%
CITY (URB + DOM)	Zinc (dissolved)	U-ZN	AA-EQS	0%	5%
CITY (URB + DOM)	Aluminum	U-ALU	AA-EQS	0%	4%
CITY (URB + DOM)	HHCB (Galaxolide)	D-HHCB	AA-EQS	0%	92%
CITY (URB + DOM)	Erythromycin Sulfomethaxole	D-SMX	AA-EQS	0%	83%
CITY (URB + DOM)	Ethinylestradiol	D-EE	AA-EQS	0%	80%
CITY (URB + DOM)	Zinc oxide	D-ZnO	AA-EQS	0%	73%
CITY (URB + DOM)	Caffeine	D-CAF	AA-EQS	0%	53%
CITY (URB + DOM)	Carbamazepine	D-CMZ	AA-EQS	0%	35%
CITY (URB + DOM)	Zinc acetate	D-ZnA	AA-EQS	0%	0%
CITY (URB + DOM)	Methylisothiazolinone	D-MI	AA-EQS	0%	0%
CITY (URB + DOM)	1-OH-Benzotriazole	D-BTZ	AA-EQS	0%	0%
CITY (URB + DOM)	Linear Alkylbenzene Sulfonate (C11.6)	D-LAS	AA-EQS	0%	0%
CITY (URB + DOM)	Titanium oxide	D-TiO	AA-EQS	0%	0%
CITY (URB + DOM)	Benzalkonium chloride	D-BAC	AA-EQS	0%	0%
CITY (URB + DOM)	Acesulfame	D-ACS	AA-EQS	0%	0%
CITY (URB + DOM)	Ibuprofen	D-IBU	AA-EQS	0%	0%

Metric	Chem-abbrev.	HI-Criterion
ZRQs	Mixture	SSD-NOE
Copper (dissolved)	U-CU	SSD-NOE
Deltamethrin	U-DELTA	SSD-NOE
Bifenthrin	U-BIF	SSD-NOE
Permethrin	U-PER	SSD-NOE
Zinc (dissolved)	U-ZN	SSD-NOE
Iron (dissolved)	U-FE	SSD-NOE
Benz(a)anthracene	U-BaA	SSD-NOE
Aluminum	U-ALU	SSD-NOE
Fluoranthene	U-FLUO	SSD-NOE
Ibuprofen	D-IBU	SSD-NOE
HHCB (Galaxolide)	D-HHCB	SSD-NOE
Ethinylestradiol	D-EE	SSD-NOE
Caffeine	D-CAF	SSD-NOE
1-OH-Benzotriazole	D-BTZ	SSD-NOE
Zinc oxide	D-ZnO	SSD-NOE
Carbamazepine	D-CMZ	SSD-NOE
Erythromycin Sulfomethaxol	D-SMX	SSD-NOE
Nonylphenol ethoxylate	U-NP1EO	SSD-NOE
Zinc acetate	D-ZnA	SSD-NOE
Titanium oxide	D-TiO	SSD-NOE
Methylisothiazolinone	D-MI	SSD-NOE
Linear Alkylbenzene Sulfonat	D-LAS	SSD-NOE
Acesulfame	D-ACS	SSD-NOE
Benzalkonium chloride	D-BAC	SSD-NOE

Scenario	Metric	Chem-abbrev.	HI-Criterion	Max (Σ)HI	Day (Σ)HI > 1	Metric	Chem-abbrev.	HI-Cri
Mixed	ΣRQs	Mixture	AA-EQS	192820	6950	ΣRQs	Mixture	SSD-NO
Mixed	Deltamethrin	U-DELTA	AA-EQS	72%	5%	Copper (dissolved)	U-CU	SSD-NO
Mixed	Iron (dissolved)	U-FE	AA-EQS	24%	5%	Deltamethrin	U-DELTA	SSD-NO
Mixed	Permethrin	U-PER	AA-EQS	3%	5%	Bifenthrin	U-BIF	SSD-NO
Mixed	Bifenthrin	U-BIF	AA-EQS	1%	5%	Permethrin	U-PER	SSD-NO
Mixed	Fluoranthene	U-FLUO	AA-EQS	0%	5%	Zinc (dissolved)	U-ZN	SSD-NO
Mixed	Nonylphenol ethoxylate	U-NP1EO	AA-EQS	0%	5%	Iron (dissolved)	U-FE	SSD-NO
Mixed	Benz(a)anthracene	U-BaA	AA-EQS	0%	5%	Benz(a)anthracene	U-BaA	SSD-NO
Mixed	Cypermethrin	A-CYP	AA-EQS	0%	15%	Aluminum	U-ALU	SSD-NO
Mixed	Copper (dissolved)	U-CU	AA-EQS	0%	5%	Ibuprofen	D-IBU	SSD-NO
Mixed	Zinc (dissolved)	U-ZN	AA-EQS	0%	5%	HHCB (Galaxolide)	D-HHCB	SSD-NO
Mixed	Pendimethalin	A-PEND	AA-EQS	0%	14%	Fluoranthene	U-FLUO	SSD-NO
Mixed	Flufenacet	A-FLUF	AA-EQS	0%	2%	Ethinylestradiol	D-EE	SSD-NO
Mixed	Aluminum	U-ALU	AA-EQS	0%	3%	Caffeine	D-CAF	SSD-NO
Mixed	HHCB (Galaxolide)	D-HHCB	AA-EQS	0%	46%	1-OH-Benzotriazole	D-BTZ	SSD-NO
Mixed	Mesosulfuron-methyl	A-MESO	AA-EQS	0%	0%	Zinc oxide	D-ZnO	SSD-NO
Mixed	Fluoxastrobin	A-FLUO	AA-EQS	0%	2%	Chlorothalonil	A-CHLOR	SSD-NO
Mixed	Erythromycin Sulfomethaxole	D-SMX	AA-EQS	0%	20%	Carbamazepine	D-CMZ	SSD-NO
Mixed	Ethinylestradiol	D-EE	AA-EQS	0%	16%	Cypermethrin	A-CYP	SSD-NO
Mixed	Zinc oxide	D-ZnO	AA-EQS	0%	10%	Erythromycin Sulfomethaxol	D-SMX	SSD-NO
Mixed	Caffeine	D-CAF	AA-EQS	0%	4%	Nonylphenol ethoxylate	U-NP1EO	SSD-NO
Mixed	Chlorothalonil	A-CHLOR	AA-EQS	0%	0%	Zinc acetate	D-ZnA	SSD-NO
Mixed	Carbamazepine	D-CMZ	AA-EQS	0%	2%	Pendimethalin	A-PEND	SSD-NO
Mixed	Epoxiconazole	A-EPOX	AA-EQS	0%	0%	Flufenacet	A-FLUF	SSD-NO
Mixed	Boscalid	A-BOS	AA-EQS	0%	0%	Titanium oxide	D-TiO	SSD-NO
Mixed	Zinc acetate	D-ZnA	AA-EQS	0%	0%	Methylisothiazolinone	D-MI	SSD-NO
Mixed	Pyraclostrobin	A-PYRA	AA-EQS	0%	0%	Linear Alkylbenzene Sufonat	D-LAS	SSD-NO
Mixed	1-OH-Benzotriazole	D-BTZ	AA-EQS	0%	0%	Epoxiconazole	A-EPOX	SSD-NO
Mixed	Methylisothiazolinone	D-MI	AA-EQS	0%	0%	Boscalid	A-BOS	SSD-NO
Mixed	Prochloraz	A-PROCH	AA-EQS	0%	0%	Prochloraz	A-PROCH	SSD-NO
Mixed	Linear Alkylbenzene Sufonate (C11.6)	D-LAS	AA-EQS	0%	0%	Pyraclostrobin	A-PYRA	SSD-NO
Mixed	Titanium oxide	D-TiO	AA-EQS	0%	0%	Acesulfame	D-ACS	SSD-NO
Mixed	Benzalkonium chloride	D-BAC	AA-EQS	0%	0%	Benzalkonium chloride	D-BAC	SSD-NO
Mixed	Acesulfame	D-ACS	AA-EQS	0%	0%	Fluoxastrobin	A-FLUO	SSD-NO
Mixed	Proquinazid	A-PROQ	AA-EQS	0%	0%	Proquinazid	A-PROQ	SSD-NO
Mixed	Prothioconazole	A-PROT	AA-EQS	0%	0%	Mesosulfuron-methyl	A-MESO	SSD-NO
Mixed	Ibuprofen	D-IBU	AA-EQS	0%	0%	Prothioconazole	A-PROT	SSD-NO
Mixed	Iodosulfuron-methyl	A-IODO	AA-EQS	0%	0%	Iodosulfuron-methyl	A-IODO	SSD-NO

S.I. Table 12. Prioritization of the relative role of chemicals in mixtures, explored via different prioritization questions, e.g., regarding the use of regulatory criteria or ecotoxicological endpoints (left and right tables) and regarding relative contributions of chemicals during peak exposures (left column within tables) or relative frequency of a compound on multiple days when HI>1 was observed.

ACKNOWLEDGMENTS

European surface water concentration data were downloaded from the NORMAN EMPODAT database (<http://www.norman-network.net/empodat/>).

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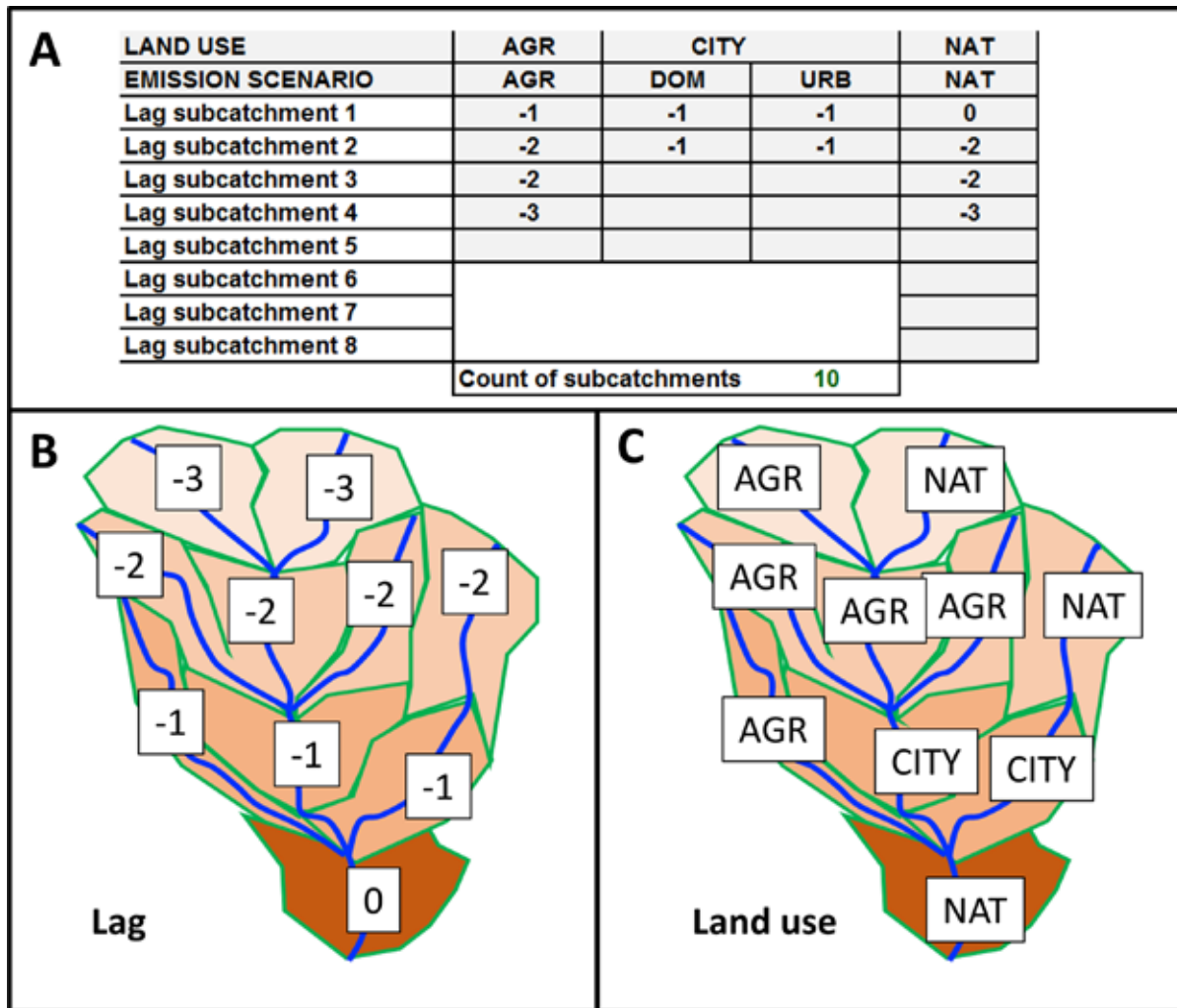


Figure 1

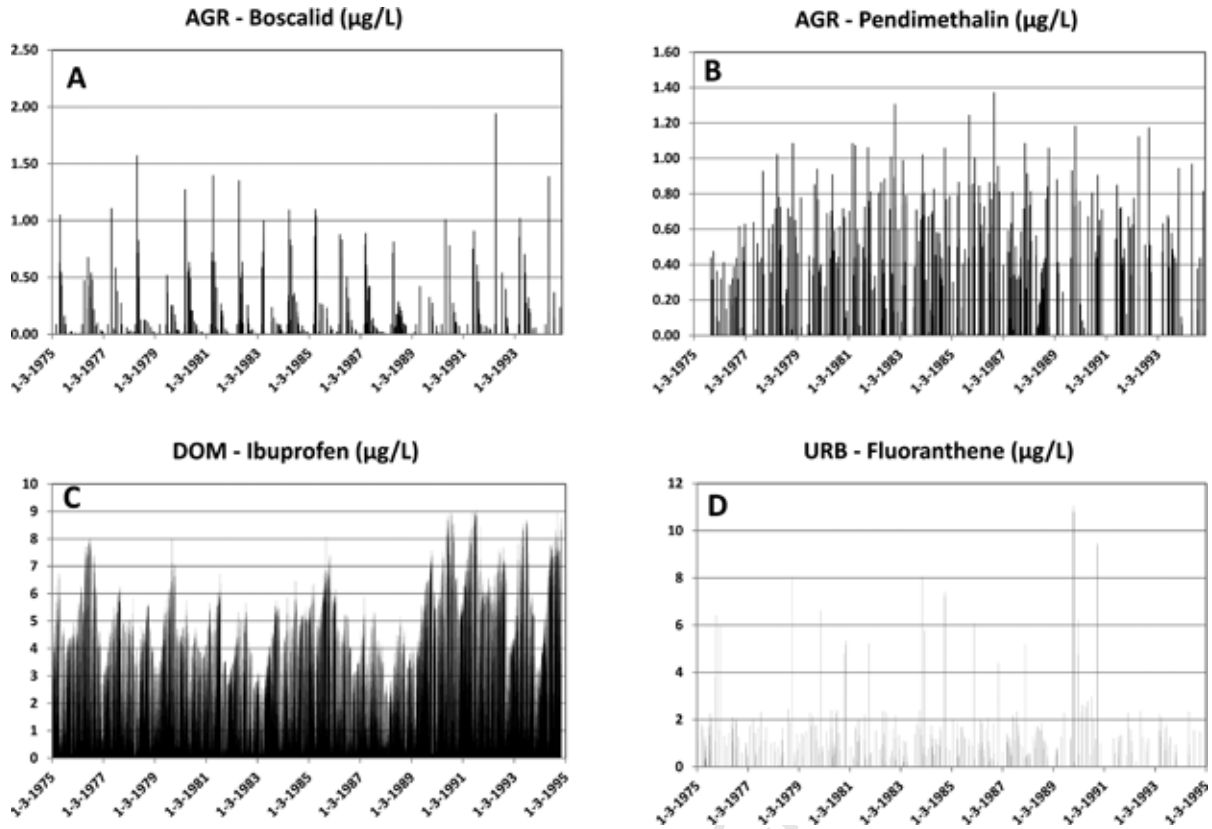


Figure 2

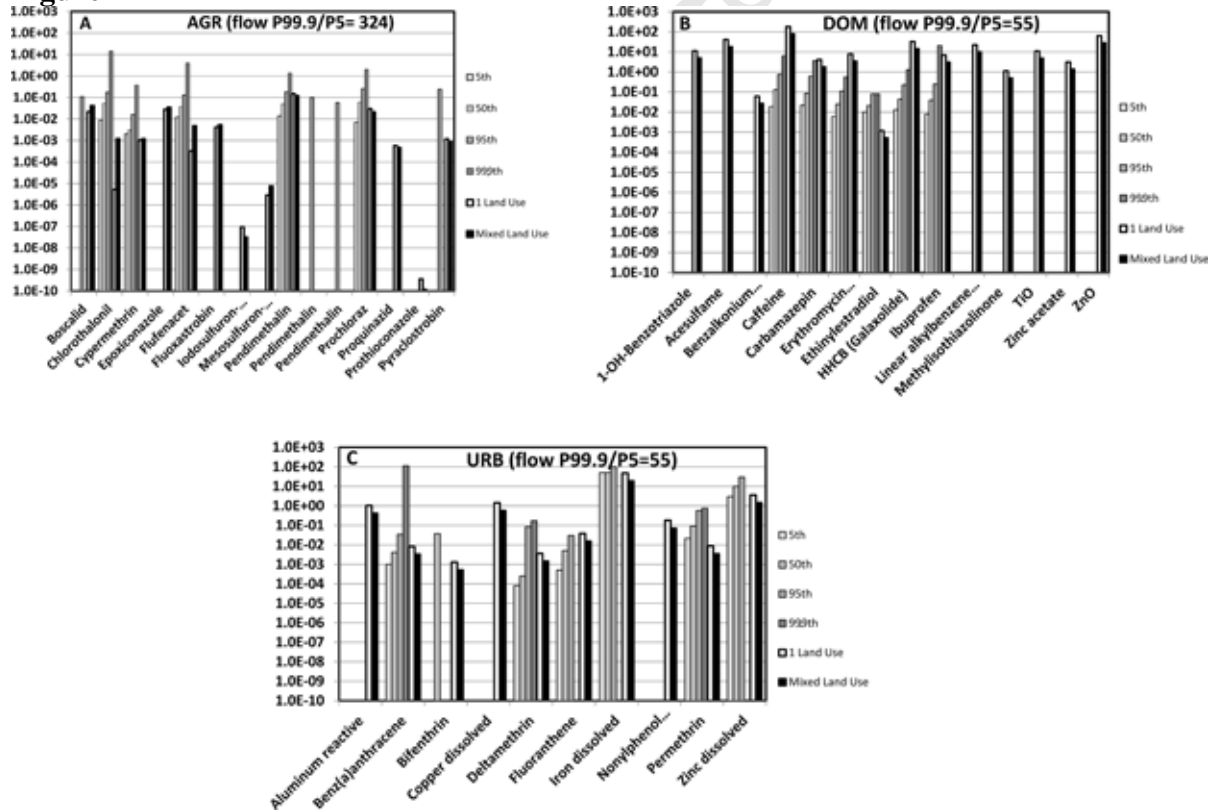


Figure 3

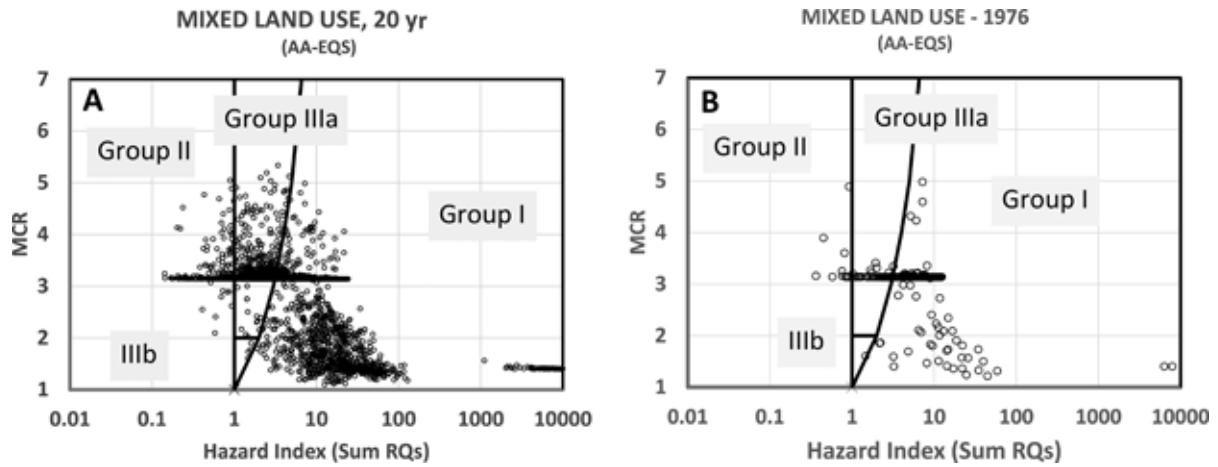


Figure 4

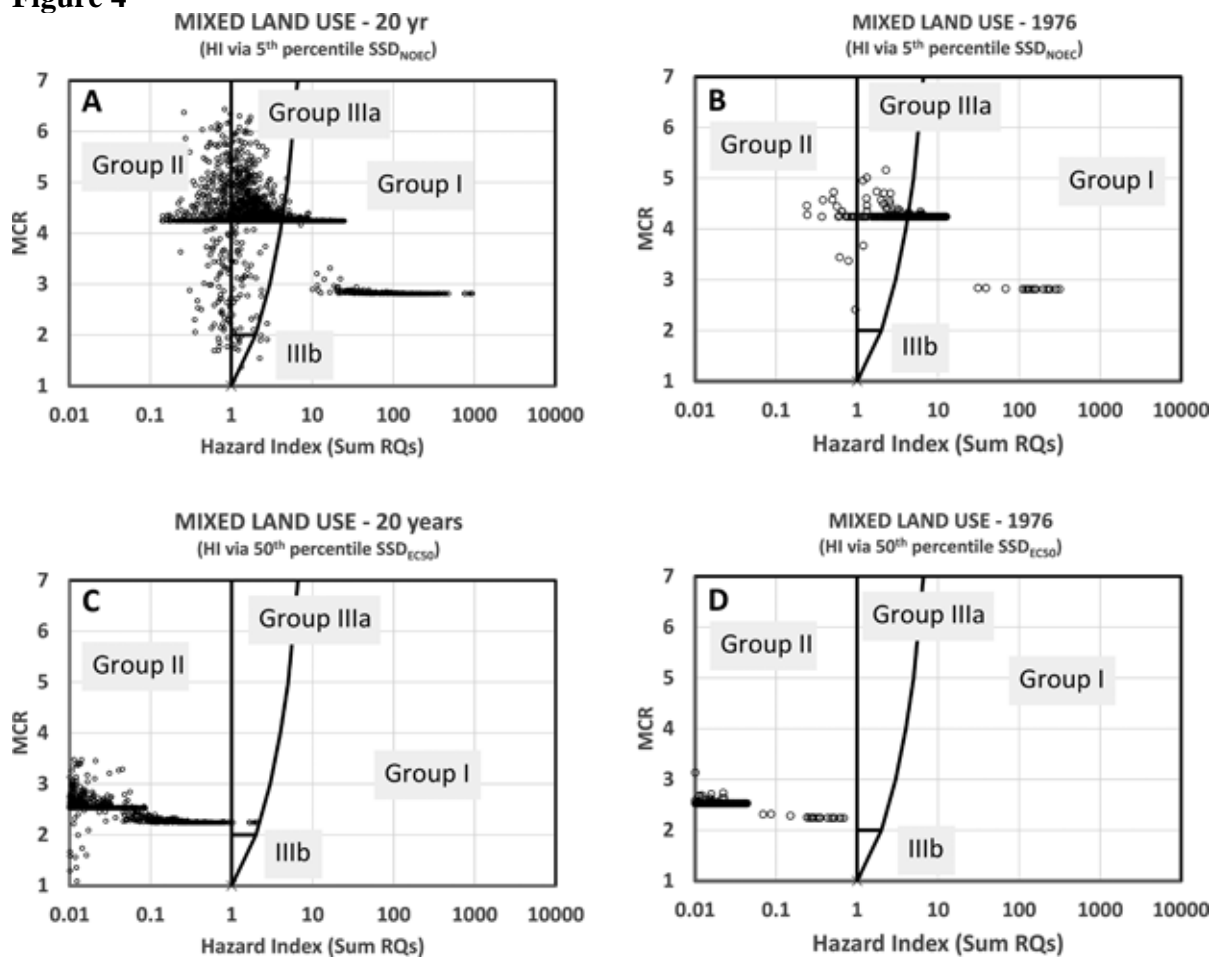


Figure 5

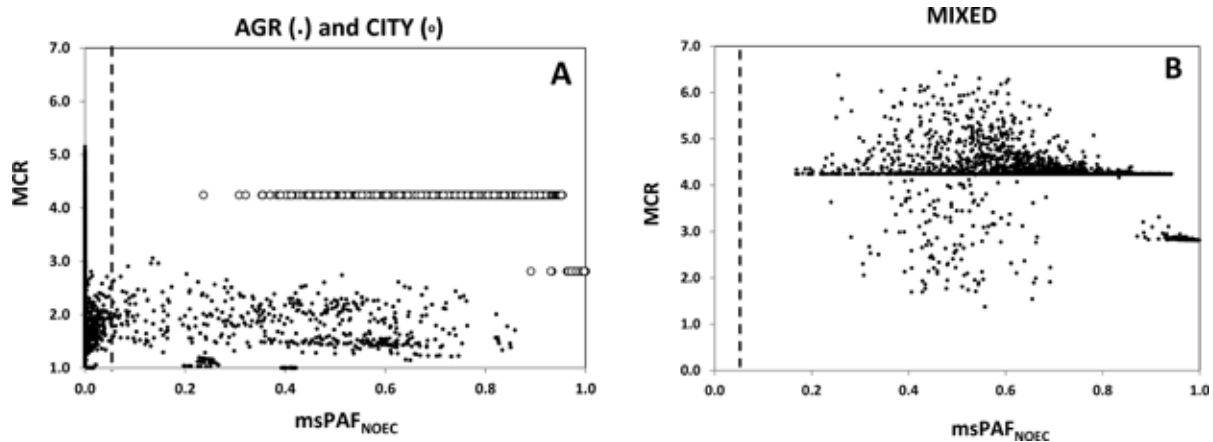


Figure 6

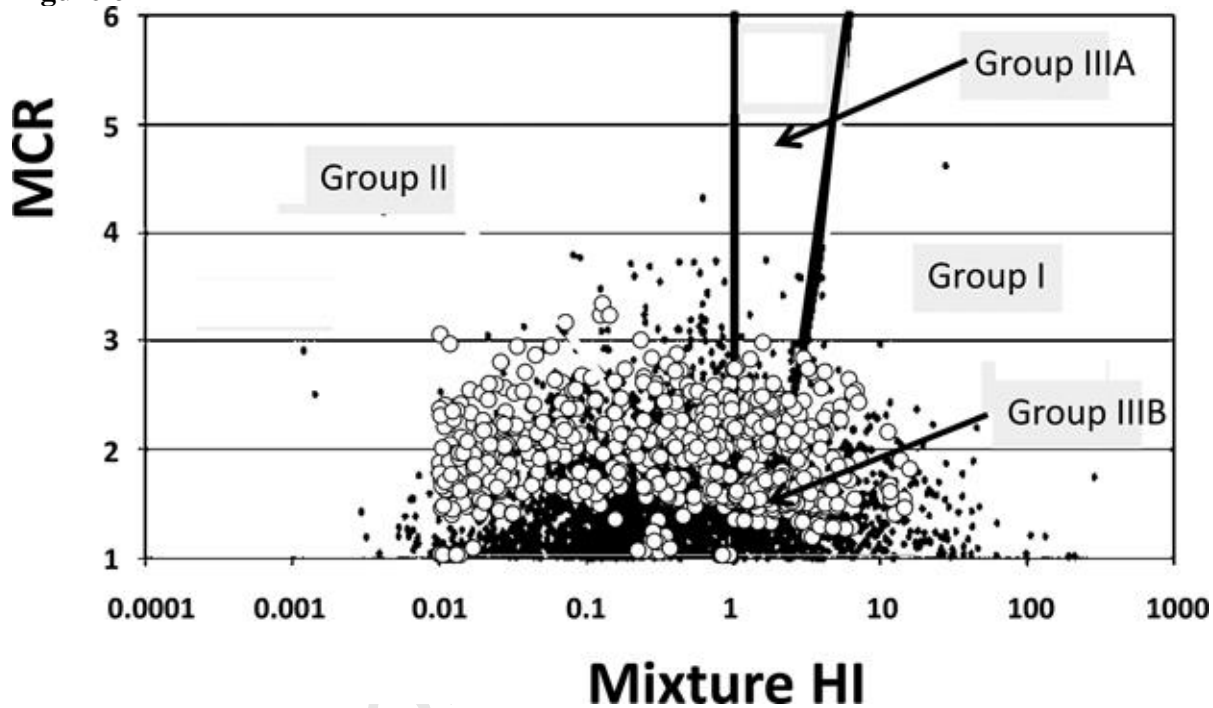


Figure 7

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