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Mixtures of chemicals are important drivers of impacts on ecological status in European surface waters

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Abstract

The ecological status of European surface waters may be affected by multiple stressors including exposure to chemical mixtures. Currently, two different approaches are used separately to inform water quality management: the diagnosis of the deterioration of aquatic ecosystems caused by nutrient loads and habitat quality, and assessment of chemical pollution based on a small set of chemicals. As integrated assessments would improve the basis for sound water quality management, it is recommended to apply a holistic approach to integrated water quality status assessment and management. This allows for estimating the relative contributions of exposure to mixtures of the chemicals present and of other stressors to impaired ecological status of European water bodies. Improved component- and effect-based methods for chemicals are available to support this. By applying those methods, it was shown that a holistic diagnostic approach is feasible, and that chemical pollution acts as a limiting factor for the ecological status of European surface waters. In a case study on Dutch surface waters, the impact on ecological status could be traced back to chemical pollution affecting individual species. The results are also useful as calibration of the outcomes of component-based mixture assessment (risk quotients or mixture toxic pressures) on ecological impacts. These novel findings provide a basis for a causal and integrated analysis of water quality and improved methods for the identification of the most important stressor groups, including chemical mixtures, to support integrated knowledge-guided management decisions on water quality.

Challenge

The Water Framework Directive (WFD) [1] has been composed to achieve good water body status and follows a stepwise assessment and management cycle [2]. Today's water quality status is often insufficient [3] demanding for a diagnostic *Assessment of Impacts* (WFD Annex II) and for programs of measures to improve water quality [4]. Ranking the role of stressors in their contribution to impacts in the diagnostic step is key for the derivation of cost-effective programs of measures. The diagnosis of impacts may use monitoring data and other data [2], and the European Commission aims at high-quality

diagnostic outputs to avoid ill-founded measures [5]. However, the currently applied diagnostic assessment of impacts [6] is not fit-for-purpose for several reasons:

- Guidance documents on water quality assessment mainly focus on the classification of chemical and ecological status, but provide limited guidance on diagnosis of the magnitude and probable causes of impacts on aquatic ecosystems.
- 2. The diagnosis currently considers chemical pollution separate from other stressors, which hampers the integrated diagnosis of impacts and probable causes.
- 3. The assessment does not reflect the complex chemical pollution in European water bodies, focusing on too few chemicals and neglecting mixtures.
- 4. The current approach does not differentiate between lower and higher mixture impacts and does nei-

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ther prioritize sites or pollution sources that require action, nor management and abatement measures.

Currently used methods classify chemical pollution in two classes based on compliance or exceedance of environmental quality standard (EQS) for measured individual chemicals according to the "one-out-all-out" principle. This is done for both priority substances (PS) and for river basin-specific pollutants (RBSP), that are considered of Europe-wide and river basin-specific concern, respectively (a few hundreds of compounds in total [3]). Regarding impacts, the ecological status distinguishes five classes, where exposures to stressors outside the naturally occurring ranges are considered to imply impacts. That these assessment methods for chemicals and other stressors must deliver different types of information as well as different specificity for management follows directly from the distinction of the two and five classes, respectively, whereby it should be further noted that chemicals are judged based on insights derived from (eco)toxicity data, and the other stressors via analysis of field monitoring data.

The selection of efficient abatement options via prioritization of information sources of similar kinds demands for a comprehensive diagnosis of all stressors when water quality appears to be affected [7-10], resulting in a rank order of all stressors—including mixtures—regarding their relative influence on water quality. As the Classification and Labeling Inventory of the European Chemicals Agency currently contains more than 145,000 compounds [11], there is also a need to expand the chemical assessment beyond the approx. 300 substances considered now [12]. Moreover, mixture impacts should be considered [13]. Given the low coverage of the registered and probably used compounds in Europe (0.2% regarding the number of compounds) and the neglect of mixture effects, the likelihood of failing to reach good water body status due to chemical pollution is currently likely underestimated.

Thus, major challenges to be addressed to improve water quality assessment and management are twofold. First, it is needed to assess complex chemical pollution in a comprehensive manner (WFD-Articles 2.31 and 2.33). Second, it is needed to consider chemical pollution and other stressors simultaneously in impact diagnosis (WFD-Annex II). This would allow for an alignment of chemical pollution and ecological status assessment, followed by a comprehensive impact assessment (diagnosis).

Research in the EU integrated project SOLUTIONS (http://www.solutions-project.eu) has resulted in a set of complementary tools and services to address these challenges, including chemical analytical screening techniques [7], improved component-based methods [8],

effect-based methods [14], and exposure and impact modeling [9]. In collaboration with the EU integrated project MARS (http://www.mars-project.eu), we applied these methods to quantify expected mixture impacts on species assemblages [15] and explored its association with the magnitude of impacts, characterized by less-than-good ecological status (cf. WFD-Annex II).

Recommendations

- Implement a holistic approach to stressor identification and management, which includes chemical pollution and other stressors, as impact assessment and efficient abatement require to deal with the ecological status and (a better defined) chemical status (considering complex mixtures) in an integrated way and not in isolation. Recognize that compliance with perchemical environmental quality standards is no adequate predictor for the magnitude of mixture impacts in aquatic ecosystems. The impacts of chemical pollution may substantially exceed the impact expected from the small set of currently considered and separately assessed compounds. This has been shown frequently, for example, for pesticide mixtures in Swiss rivers [16].
- Inform target-oriented, efficient and cost-effective water quality management with holistic assessments to evaluate the status of protection (reference conditions) and characterize the magnitude of impacts to focus management efforts on the actual drivers of the impairment of water quality, ecological status and ecosystem services.
- Align sampling sites and dates of ecological and chemical water quality monitoring and establish common data repositories and evaluation to enable the comprehensive diagnostic assessments. Consider that this pertains to the raw monitoring data, and not to the WFD-ecological and chemical status classification; summarizing data in classes removes valuable information for impact diagnosis. Exploring the role of mixtures as potential stressor variable can start with simple visual data plotting inspections (whereby quantile regression principles suggest that the observation of a decreasing trend in Y-values (e.g., ecological status) with increasing X-values (e.g., chemical pollution) indicates that X acts as a limiting factor), but can be expanded with more dedicated statistical methods when needed.

Following these recommendations will help with prioritizing water bodies regarding expected impacts of mixtures and other stressors on aquatic species assemblages, followed by a prioritization of dominant chemicals within

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the mixtures occurring in those water bodies. This component-based assessment can be combined with other lines of evidence, such as the results effect-based monitoring (as described in [14]).

Requirements

Building forth on recommendations to expand on the number of chemicals and mixtures to be considered [8, 10, 14], an effective implementation towards forwarding water quality improvement via improved assessment and management planning requires:

- Novel guidance on the Assessment of Impact-step of the WFD Annex II, especially on the integrated assessment of the likelihoods of all stressors (including pollutants and their mixtures) to cause harm"; updating the current Guidance Document on the analysis of pressures and impacts [6] would be suitable.
- Utilization of improved component- and effect-based methods [8, 14, 17], to support the meaningful alignment of ecological and chemical pollution data, considering the policy environmental objectives of both protection (when biological quality elements are in reference condition) and restoration (when impacts are observed, and/or exposures exceed the no-effect level).
- Inter-calibration of chemical and ecological data (with novel data and published case studies shown below), across data sets on chemicals, biological quality elements, taxonomic groups, regions and water body types studied so far, to calibrate predicted to observed impacts, and to derive chemical pollution classes and class boundaries that correspond with ecological impacts and ecological status boundaries.
- At the institutional level, it is key to align the approaches developed in the WFD-Common Implementation Working Groups 'Chemicals' and 'Ecological status', covering both component- and effect-based methods for assessing chemical pollution.
- Arrange bringing together (spatially) aligned monitoring data on chemicals (plus factors that determine their bioavailability), other quality elements and ecological data, to enable deriving optimal insights into all potential causes of impacts.
- Storage of raw data for the assessments is needed, rather than of the frequently used format of ecological and chemical status data; useful details in the original monitoring data are removed in the steps between raw data and the classification of the ecological and chemical status of water bodies.

As yet, the WFD Annex II text [1] provides the mandate for the recommended refined pollution impact diagnosis via pertinent approaches. Thus, monitoring can be complemented with modeling of exposure to chemical mixtures and of impacts. Guidance on the suggested methods is helpful to improve the understanding of water managers that chemical pollution encompasses all chemicals and their mixtures (Article 2.31 and 2.33) beyond the current emphasis on priority substances and river basin-specific pollutants, as recognized in an early-stage policy implementation [6]. The guidance can describe that new and effective chemical pollution diagnostic methods are currently available and also how they serve the policy goals [18]. The recommended approaches can be applied by water quality managers for executing the diagnostic Assessment of Impacts step. Upon calibrating the mixture impact metrics to the ecological impact levels, the mixture impact metrics can be used to derive the likelihood that mixtures affect the ecological status.

Achievements

We evaluated the conceptual differences between ecological and chemical assessments, addressed the differences, and aligned those using improved component-based methods for chemical pollution assessment [8], and developed an integrated approach for the diagnosis of the contributions of all stressors (including chemical pollution) to ecological impacts. This was a follow-up of explicit ambitions of the European Union formulated for novel research on water resources [19], as elaborated in the call for proposals of both projects (see Appendix 1 of [2]). The collaborative efforts resulted in the following achievements.

Defining the mixture impact metric that should be aligned with ecological data

An innovative tiered framework and methods to predict the impact of chemical mixtures were designed and tested, with ecotoxicity data made available for over 12,000 chemicals [8, 15, 20]. The methods that can be utilized for mixture assessments are summarized in a related Policy Brief [8], based on contemporary opportunities to use available (eco)toxicity data and the classical mixture models of concentration addition (CA) and response addition (RA) for the current purposes. The improved component-based approaches vastly expand our potential to assess chemical pollution impacts on species assemblages and ecological status. The methods can be applied to evaluate mixture impacts from measured or predicted environmental concentrations of chemicals. The methods can be employed on extensive monitoring data sets. Options are the NORMAN database (https://www.norman-network.com/nds/empodat/)

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and the IPChem database (https://ipchem.jrc.ec.europ a.eu/RDSIdiscovery/ipchem/index.html). Moreover, an integrated emission-fate-impact 'model train' has been developed and implemented to provide Europe-wide predicted concentrations of more than 1800 compounds [9]. These measured or predicted data do not only allow for ranking of expected mixture impact metrics across water bodies and amongst chemicals within mixtures, but they also allow for aligning chemical pollution metrics with ecological monitoring data and ecological status classifications.

Correlation of mixture impacts, ecological impacts and ecological status

An array of statistical techniques has been employed aligning chemical pollution data, e.g., in the format of mixture toxic pressure (multi-substance potentially affected fraction, msPAF) metric, with data from ecological monitoring. Thereafter, various statistical techniques can be applied to investigate whether and in how far increased toxic pressure relates to alterations in aquatic ecosystems. It should be explicitly noted that statistical associations, when found, do not imply causation. Strict causal evidence is, however, not required: the WFD Annex II and the pertinent guidance defines that the target of assessments is to assess the likelihood that stressors may cause an impact [1, 21], to be established by one or more lines of evidence.

Amongst the simple and intuitively clear methods is the plotting of the raw data, (optionally) followed by quantile regression [22]. With a potential stressor variable plotted as X-variable, the decrease of an ecological impact variable (Y) with increasing X is interpreted simply as evidence that X likely acts as a factor limiting Y. Evidently, such results should be interpreted with care,

that is: researchers should check on covariation of factor X with other factors. If X highly correlates with another factor (C, the covariant), the limitation could also be attributable to C, or to X and C combined.

This principle was used in two studies, in which a covariation check showed non-significant covariation of mixture toxic pressure with other monitored variables. First, ecological impacts on the abundance of individual taxa were studied using monitoring data for both chemicals and species abundances for the Netherlands. Here, we illustrate that raw data already show a clear pattern, with increasing X associated with a decreasing upper bound of the Y-data (Fig. 1, left). The X-value is the mixture toxic pressure of the chemicals found at the monitoring sites (msPAF-EC50 [8, 15]), and the Y-value is the abundance of the taxon; the dots are the XY-values of the nearly 6000 sampling sites. Clearly, increased mixture exposure limits the abundance of an example taxon (data shown for Gammarus spec.). Visual inspection of plotted data already shows that chemical pollution is likely a factor that limits high abundances of the species. Note that the *Y*-values for a narrow mixture toxic pressure (*X*) range can vary substantially, related to the effects of other stressors on abundance [23]. According to the principles of quantile regression [22], the data-poor upper right corner of the example graphs is evidence for chemical mixtures acting as factor limiting taxon abundance. Likewise, but now for lowland rivers at the European scale and looking at predicted environmental concentrations of 24 priority substances [9], there is evidence for chemical mixtures of these priority substances acting as factor limiting the ecological status as defined in the WFD. In this case, we plotted the P95 of the Y-values per bin of X-data; the raw data distribution is not plotted, but it resembles the spread of data of sub-figure A (Fig. 1, right). More

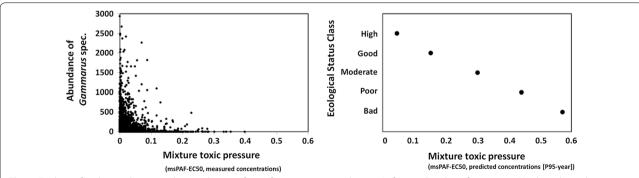


Fig. 1 Evidence for chemical mixtures being a limiting factor for two impact endpoints. Left: area: Dutch surface waters; X-values derived from measured concentrations of chemicals in the Netherlands; Y-values are abundance data for an example taxon; dots: raw XY-data (nearly 6000 sites). Right: Area: European lowland rivers with a catchment area > 100 km² (approx. 14,000 sites); X-values derived from predicted environmental concentrations of 24 priority substances [9], summarized as 95th percentile X-values within the ecological status classes; Y-values are WFD-ecological status classes (based on monitoring data)

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complex statistical methods can be employed, to describe the association between the response metric (*Y*) and the set of monitored potential stressor variables. Examples of such studies have shown that mixture toxic pressure is a factor that statistically covaries with abundance change of the majority of species (e.g., [24, 25]), and that indeed the abundance variation for a majority of species is related to a set of stressors (including mixtures). Ongoing studies corroborate and refine these findings for more complex mixtures, whereby variability in ecological attributes of European surface waters can be statistically attributed for approx. 1/3rd to mixtures in a case study that considered approx. 1800 compounds.

Calibration of predicted chemical pollution impacts to observed ecological impacts

The findings shown in Fig. 1 summarize a larger array of similar observations for other data sets (other species groups, other geographies, other chemicals and different other stressors, e.g., [25, 26]) or study types (e.g., [27, 28]). The results obtained from the other studies all imply that chemical pollution with mixtures appear to limit the ecological performance (from species abundance to integrated ecological status as response variables) in chemical-exposed aquatic ecosystems. In all studies, the check for covariation between the mixture exposure metric and other measured potential stressor variables suggested that the findings could not be attributed to the other variables (low or negligible covariation). This kind of relationship is not found when the same data are used in combination with the current classification of chemical pollution (expressed as the two classes), due to the various endpoints and assessment factors underlying the definition of the environmental quality standards, and the fact the ecological impacts will not immediately occur when such protective standards are exceeded. Or stated differently: it cannot easily be envisaged how a two-class stressor system for chemical pollution (X) would meaningfully relate to a five-class ecological impact system.

The results of recent analyses of monitoring data provide some additional insights that are relevant for practice. That is, although the studies show that mixture impacts are important, they also show that frequently some chemicals have a relatively dominant role (e.g., [15, 29–31]). This was also found in scenario studies [32]. It is not surprising that a few, or even one, chemicals may be dominant in causing adverse effects, as the opposite can be deducted as unlikely (all chemicals a nearly equal role). It should be noted, however, that the dominance of some chemicals is the key phenomenon, but that the identity of the dominant chemicals is spatiotemporally variable.

Observations such as those in Fig. 1 imply that it is possible to calibrate the predicted impacts—using the improved component-based methods [8] or the effect-based methods [14]—on observed effects of mixtures in the field. As yet, the number of this kind of observations is relatively limited, but with further studies it will be possible to align the five ecological status classes to an equal number of newly defined chemical pollution classes. This would solve the practical problems encountered with the current chemical pollution assessment.

Implications for protection, restoration and management

The collaboration between ecotoxicologists and ecologists provided highly relevant insights, showing that an integrated and meaningful impact diagnosis of water quality can be implemented. That is, water quality managers can be served by a comprehensive assessment of water quality in which all stress factors are ranked; this can replace or add to the information gained from the currently separated assessments. When considering implementation, the research stage utilizes existing monitoring data, which are, thus, used more effectively. The implementation stage could differ, depending on scale. For the EU-scale, implementation could consist of using the mixture impact scales after wider calibration to the ecological impact scale. For regional water quality management, various data sets may be sufficient for exploratory analyses on chemicals as limiting factor, via, e.g., the simple data plotting and quantile regression (as in Fig. 1). It should be noted, however, that the current examples show that the method is feasible, but not that it is without problems. A key problem is, for example, to create a proper dataset, with co-located information for chemicals, other stressors and ecological endpoints. Upon the integrated diagnosis, a wide array of management options can be employed for protection or restoration [33], but management may be costly. A good diagnosis of likely impacts and a prioritization of impacted sites and underlying stressors is crucial for (cost-)effective water quality management [5]. Whereas the WFD-environmental objectives 'prevention' (Article 4.1.a.i) can remain to be evaluated utilizing protective environmental quality standards, the WFD-objective of 'restoration' as required for cases where ecological impacts are observed (Article 4.1.a.ii) is better served by an integrated diagnostic assessment involving chemical pollution and other stressors.

The results of the diagnostic studies illustrate that chemical pollution stress can be aligned with other stressor data and with biomonitoring data to support water quality assessment and management. The investigated approach addresses some key problems of the current approach, but is surely not the only thinkable

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approach. We present only results from the investigated option, building forth on the fact that large investments in monitoring provide us with large monitoring data sets. The presented methods show that there is substantial latitude for improved and useful analysis of such data. Evidence from further calibration efforts between predicted chemical impacts and observed ecological impacts would provide additional support for interpretation, acceptance, and communication of the present outcomes of the comprehensive assessment approach to diagnosis.

Abbreviations

CA: concentration addition; EQS: environmental quality standard; ms-PAF: multi-substances potentially affected fraction; PS: priority substance; RA: response addition; RBSP: river basin-specific pollutant; WFD: Water Framework Directive.

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References

- EC (2000) Directive 2000/60/EC of the European parliament and of the council of 23 October 2000 establishing a framework for community action in the field of water policy. Off J Eur Communities L 2000(327):1–72
- Posthuma L et al (2019) A holistic approach is key to protect, monitor, assess and manage chemical pollution of European surface waters. Environ Sci Eur. https://doi.org/10.1186/s12302-019-0243-8
- EEA (2018) European waters—assessment of status and pressures. 2018, EEA Report No 7/2018. EEA, Copenhagen
- Elosegi A, Gessner MO, Young RG (2017) River doctors: learning from medicine to improve ecosystem management. Sci Total Environ 595:294–302
- EC (2015) The Water Framework Directive and the Floods Directive: actions towards the 'good status' of EU water and to reduce flood risks. European Commission, Brussels
- EC (2003) Common implementation strategy for the Water Framework Directive (2000/60/EC). Guidance Document No. 3. Analysis of Pressures and Impacts. EC, CIS-Working Group 2.1—IMPRESS, Brussels
- Brack W et al (2019) High-resolution mass spectrometry to complement monitoring and track emerging chemicals and pollution trends in European water resources. Environ Sci Eur. https://doi.org/10.1186/s1230 2-019-0230-0
- Posthuma L et al (2019) Improved component-based methods for mixture risk assessment are key to characterize complex chemical pollution in surface waters. Environ Sci Eur. https://doi.org/10.1186/s1230 2-019-0246-5
- Van Gils J et al (2019) The European Collaborative Project SOLUTIONS developed models to provide diagnostic and prognostic capacity and fill data gaps for chemicals of emerging concern. Environ Sci Eur. https://doi. org/10.1186/s12302-019-0248-3
- Kortenkamp A et al (2019) Mixture risks threaten water quality: the European Collaborative Project SOLUTIONS recommends changes to the WFD and better coordination across all pieces of European chemicals legislation to improve protection from exposure of the aquatic environment to multiple pollutants. Environ Sci Eur. https://doi.org/10.1186/ s12302-019-0245-6
- ECHA (2019) https://echa.europa.eu/information-on-chemicals/cl-inventory-database. Accessed 8 Aug 2019
- Arle J, Mohaupt V, Kirst I (2016) Monitoring of surface waters in Germany under the Water Framework Directive—a review of approaches, methods and results. Water 8(6):217
- 13. Kortenkamp A, Backhaus T, Faust M (2009) State of the art report on mixture toxicity. EC: Directorate General for the Environment, Brussels
- Brack W et al (2019) Effect-based methods are key. The European Collaborative Project SOLUTIONS recommends integrating effect-based methods for diagnosis and monitoring of water quality. Environ Sci Eur 31(1):10
- Posthuma L et al (2019) Species sensitivity distributions for use in environmental protection, assessment, and management of aquatic ecosystems for 12,386 chemicals. Environ Toxicol Chem 38(4):905–917
- Moschet C et al (2014) How a complete pesticide screening changes the assessment of surface water quality. Environ Sci Technol 48(10):5423–5432
- Brack W et al (2019) Effect-based methods are key. The European Collaborative Project SOLUTIONS recommends integrating effect-based methods for diagnosis and monitoring of water quality. Environ Sci Eur 31:10
- Brack W et al (2019) Let us empower the WFD to prevent risks of chemical pollution in European rivers and lakes. Environ Sci Eur 31(1):47
- EU (2010) The "Innovation Union"—turning ideas into jobs, green growth and social progress. 2010: IP/10/1288, 6th October 2010, Brussels, Belgium
- Kortenkamp A et al (2018) Common assessment framework for HRA and ERA higher tier assessments including fish and drinking water and multi-species ERA via SSD, population-level ERA via IBM and food web vulnerability ERA. SOLUTIONS Deliverable D18.1
- 21. EC (2005) Common implementation strategy for the Water framework Directive (2000/60/EC)—Guidance Document No. 13—overall approach to the classification of ecological status and ecological potential, European Commission, Editor, Brussel, Belgium
- 22. Cade BS, Noon BR (2003) A gentle introduction to quantile regression for ecologists. Front Ecol Environ 1(8):412–420

Posthuma et al. Environ Sci Eur (2019) 31:71 Page 7 of 7

- 23. Grizzetti B et al (2017) Human pressures and ecological status of European rivers. Sci Rep 7(1):205
- 24. De Zwart D et al (2006) Predictive models attribute effects on fish assemblages to toxicity and habitat alteration. Ecol Appl 16(4):1295–1310
- Posthuma L et al (2016) Water systems analysis with the ecological key factor 'toxicity'. Part 2. Calibration. Toxic pressure and ecological effects on macrofauna in the Netherlands. STOWA, Amersfoort
- De Zwart D (2005) Ecological effects of pesticide use in The Netherlands: modeled and observed effects in the field ditch. Integr Environ Assess Manag 1(2):123–134
- Malaj E et al (2014) Organic chemicals jeopardize the health of freshwater ecosystems on the continental scale. Proc Natl Acad Sci 111(26):9549–9554
- Berger E et al (2016) Field data reveal low critical chemical concentrations for river benthic invertebrates. Sci Total Environ 544:864–873
- Gustavsson M et al (2017) Pesticide mixtures in the Swedish streams: environmental risks, contributions of individual compounds and consequences of single-substance oriented risk mitigation. Sci Total Environ 598:973–983

- 30. Backhaus T, Karlsson M (2014) Screening level mixture risk assessment of pharmaceuticals in STP effluents. Water Res 49:157–165
- Vallotton N, Price PS (2016) Use of the maximum cumulative ratio as an approach for prioritizing aquatic coexposure to plant protection products: a case study of a large surface water monitoring database. Environ Sci Technol 50(10):5286–5293
- Posthuma L et al (2018) Prospective mixture risk assessment and management prioritizations for river catchments with diverse land uses. Environ Toxicol Chem 37(3):715–728
- 33. Posthuma L et al (2019) Exploring the 'solution space' is key. SOLUTIONS recommends an early-stage assessment of options to protect and restore water quality regarding chemical pollution. Environ Sci Eur (submitted)

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