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POLICY BRIEF

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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

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Abstract

Evidence is mounting that chemicals can produce joint toxicity even when combined at levels that singly do not pose risks. Environmental Quality Standards (EQS) defined for single pollutants under the Water Framework Directive (WFD) do not protect from mixture risks, nor do they enable prioritization of management options. Despite some provisions for mixtures of specific groups of chemicals, the WFD is not fit for purpose for protecting against or managing the effects of coincidental mixtures of water-borne pollutants. The conceptual tools for conducting mixture risk assessment are available and ready for use in regulatory and risk assessment practice. Extension towards impact assessment using cumulative toxic unit and mixture toxic pressure analysis based on chemical monitoring data or modelling has been suggested by the SOLUTIONS project. Problems exist in the availability of the data necessary for mixture risk assessments. Mixture risk assessments cannot be conducted without essential input data about exposures to chemicals and their toxicity. If data are missing, mixture risk assessments will be biassed towards underestimating risks. The WFD itself is not intended to provide toxicity data. Data gaps can only be closed if proper feedback links between the WFD and other EU regulations for industrial chemicals (REACH), pesticides (PPPR), biocides (BPR) and pharmaceuticals are implemented. Changes of the WFD alone cannot meet these requirements. Effect-based monitoring programmes developed by SOLUTIONS should be implemented as they can capture the toxicity of complex mixtures and provide leads for new candidate chemicals that require attention in mixture risk assessment. Efforts of modelling pollutant levels and their anticipated mixture effects in surface water can also generate such leads. New pollutant prioritization schemes conceived by SOLUTIONS, applied in the context of site prioritization, will help to focus mixture risk assessments on those chemicals and sites that make substantial contributions to mixture risks.

Keywords: Mixture risk assessment, Complex mixtures of chemicals, Recommendations, Water Framework Directive

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Challenge

Aquatic wildlife and humans are simultaneously and sequentially exposed to multiple chemicals from different sources by direct uptake from water and indirectly via consumption of aquatic organisms. Scientific evidence for the toxicity from such mixtures is mounting, yet the regulatory instruments provided in the Water Framework Directive (WFD, *Commission Directive 2013/39/EU*) [1] cannot deal appropriately with this challenge. This endangers the realization of WFD protection goals. Ensuring better protection from chemical mixture risks, as well as prioritizing management plans to focus on water bodies that are most affected, will require stronger legal stimuli in the WFD, as well as better integration with other elements of the EU regulatory system.

Until about a decade ago, toxicologists, risk assessors and regulators regarded risks from chemical mixtures as negligible, as long as exposures to all single chemicals in the cocktail were below the levels judged to be safe for each chemical alone [2, 3]. However, an increasing body of scientific evidence has challenged this notion, showing that a neglect of mixture effects can cause chemical risks to be underestimated. International bodies such as the World Health Organisation now acknowledge the need for considering mixtures in chemical risk assessment and regulation [4]. Yet, despite some provisions for mixtures of chemically similar pollutants such as dioxins, brominated diphenyl ethers and certain other persistent organic pollutants, the WFD still focuses overwhelmingly on single chemical assessments.

Scientific evidence

More than 30 years ago, the first studies of toxicity from multi-component mixtures of non-reactive organics with unspecific modes of action in fish and other aquatic organisms appeared [5–8]. These publications provided first evidence for significant combined effects from mixture components at concentrations which do not cause significant effects when applied singly.

In subsequent years, further studies with more rigorous experimental designs and additional toxicity endpoints were conducted. Mixture effects occurred when each chemical was present at or below experimental NOAELs (no observed adverse effect levels) for single substances [9]. The suitability of the current Environmental Quality Standards (EQS) for protecting against mixture effects has recently been tested directly by researchers at European Commission DG JRC. Combinations of 14 or 19 pollutants at EQS levels produced significant toxic effects in microalgae, daphnids, and fish and frog embryos [10], at concentrations 100-fold or more below their individual NOAELs.

Already in 1987, on the basis of the then available mixture studies in fish, the European Inland Fisheries Advisory Commission concluded that the setting of water quality criteria for chemicals should focus on mixtures with similar modes of action, rather than on single chemicals. However, Europe-wide water quality legislation was not enacted at the time, and the framework needed for implementing these insights was not available. Partial implementation was achieved in 2000 with the WFD, which includes EQS for mixtures of specific groups of structurally similar chemicals, such as dioxins, polybrominated diphenyl ethers (PBDEs), four cyclodiene pesticides and four DDT isomers. However, to this day, the possibility of mixture effects between these groups of chemicals or between all chemicals present in the aquatic environment is not considered in practice.

Recommendations

As currently configured, the provisions of the WFD have minimal scope for the introduction of the scientific approaches that are needed for effectively addressing mixture risks, and corresponding guidance to address mixture risks is outdated. To achieve an improved level of protection, and to better manage mixture risks, changes in the WFD and in other EU regulations are required. The following improvements are recommended:

- Improve WFD technical guidance by introducing consistent and comprehensive concepts for conducting mixture risk assessment. The WFD intends to protect all receptors, including humans and wildlife from direct and indirect toxicity of chemical substances. Risk assessment approaches for single chemicals that deal with all these receptors are available [11], but a coherent framework for conducting mixture risk assessment that can address these overarching protection goals is missing. The existing guidance on conducting mixture risk assessment within the WFD [11] is outdated and should be replaced by a comprehensive mixture risk assessment framework.
- Develop and implement effective feedback loops between WFD and other EU regulations to close data gaps that block mixture risk assessment. Component-based mixture risk assessments require exposure and toxicity data for all chemicals that make up the mixture to be assessed. If such data are missing for some compounds, the assessment either stalls, or chemicals have to be left out from consideration. Inevitably, this biases the assessment towards underestimating risks. Mechanisms for closing these data gaps are not established in the WFD itself. In principle, the required data can be gathered through provisions for data and information requirements in other EU regulations such as REACH, the Plant Protection Products Regulation (PPPR) and the Biocidal Prod-

ucts Regulation (BPR). Unfortunately, REACH does not currently deliver the quality and quantity of data required even for rudimentary (mixture) risk assessments. Most of the chemical registration dossiers do not even meet basic quality requirements [12]. These deficiencies should be addressed by implementing better data and information requirements across several EU regulations that are fit for conducting mixture risk assessments.

- Exploit mixture risk assessment methods to improve the prioritization of pollutants, and water bodies within an array of monitored sites. Currently, compounds that are not WFD *priority substances* or *river basin specific pollutants* are insufficiently monitored, and compounds not subject to monitoring cannot be prioritized. This deadlock is particularly problematic with substances that make a significant contribution to mixture risks, but themselves do not exceed acceptable levels. Mixture risk assessments may help to identify such substances as candidates for pollutant prioritization. They may also help ranking impact magnitudes across water bodies, to prioritize management to those where impacts are likely largest. Effect-based assessment methods that rely on batteries of bioassays for the testing of complex mixtures can also be marshalled to identify new and emerging substances that contribute substantially to mixture risks, and sites where mixtures likely cause impacts.

Requirements

These recommendations cannot be implemented without meeting the following requirements:

- As for single chemical risk assessments under the WFD, mixture risk assessment should enable the protection and impact assessment of multiple receptors, including all relevant biological quality elements and humans. The assessment should not be restricted to just a few taxa. This requires the integration of human and ecotoxicological risk assessment in one coherent framework.
- For mixture risk assessments, minimum data and quality requirements that can be accepted as sufficient for providing a basis for risk management must be defined, just as they are established for single chemicals under the WFD.
- In defining such quality requirements, it is necessary to recognize that mixture risk assessments will have to be conducted on the basis of (eco)toxicity data Quality Standards for specific organism groups. This will avoid problems that arise when conducting mixture risk assessments on the basis of EQS or PNECs that were derived for single substances. As these values are geared towards toxicities to the most sensitive receptor, and because these receptors differ from substance to substance, the use of EQS or PNECs in mixture risk assessment may lead to logical contradictions. It does not make sense to base mixture risk assessment on toxicity values for different species with different assessment factors as this may significantly distort the assessment.

Achievements in SOLUTIONS that support these recommendations

The SOLUTIONS project has provided the scientific concepts that are needed to underpin these recommendations.

We developed an advanced framework for the assessment of ecotoxicological and human health risks from combined exposures to multiple chemicals in European surface waters. The framework presents several innovations: It implements a systematic tiering scheme that removes the distortions and uncertainties associated with widely used mixture risk assessment methods derived from concentration addition. We developed quantitative criteria that allow us to identify chemicals with high impacts on projected mixture risks, the so-called drivers [13].

The framework was evaluated in several case studies of measured water concentrations for ca. 300 pollutants in the Danube. It was highly effective in isolating sub-sets of chemicals for which the required toxicity data were available and for which mixture risks could be established with a relatively high degree of certainty.

Furthermore, taxa-specific tiered ecological and human mixture risk assessments for modelled concentrations of more than 1800 substances were carried out for the Danube, Rhine and Spanish river basins (SCARCE) on the basis of modelled water concentrations. Across all river basins, the mixture risk assessments suggest that multiple river segments are insufficiently protected from chronic impacts on algal and daphnid communities. Many chemicals not currently regulated under the Water Framework Directive (WFD) were projected to drive the associated mixture risks. For almost the entire Rhine catchment, and Western and Southern parts of the Danube basin, the analysis did not identify concerns for chronic impacts on fish, at least not for the chemicals for which relevant chronic toxicity data were available. However, indications for impacts on fish are anticipated in Spanish basins and in the Central parts of the Danube basin. In many river segments, there were indications for concerns for the water quality when used directly as a resource for drinking water. The modelled mixture

exposures that result from a standardized human consumption scenario of fish caught in rivers exceeded levels judged to be safe.

Moreover, various site-specific case studies on water samples from the rivers Danube and Rhine demonstrated the relevance of mixture consideration for explaining observable biological effects through the joint use of chemical and bioanalytical methods [14–16].

Our results suggest that WFD protection goals cannot currently be realized for combined exposures to chemicals projected to occur in European water bodies.

We also conducted a thorough examination of all available concepts and methods for the regulatory assessment of risks from chemical mixtures and the integration of such mixture risk assessment approaches into prioritization procedures [17]. None of the available approaches provides a comprehensive solution for this complex problem. Each approach has some specific advantages but also suffers from severe limitations. We synthesized the available approaches into an advanced framework for the identification of priority substances and priority mixtures. Full implementation of this framework requires changes to the legal text of the WFD, as recommended here.

Abbreviations

BPR: Biocidal Products Regulation; DDT: dichlorodiphenyltrichloroethane; EQS: Environmental Quality Standards; NOAELs: no observed adverse effect levels; PNEC: predicted no effect concentration; PBDEs: poly-brominated diphenyl ethers; PPPR: plant protection products regulations; REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals; WFD: Water Framework Directive.

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Authors' contributions

AK drafted the manuscript. MF conducted a great deal of the underlying conceptual and analytical work. TB, RA, MS, CM, SE, LP and WB further improved the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

The details of the underpinning analyses will be published in due course; manuscripts are in preparation.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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