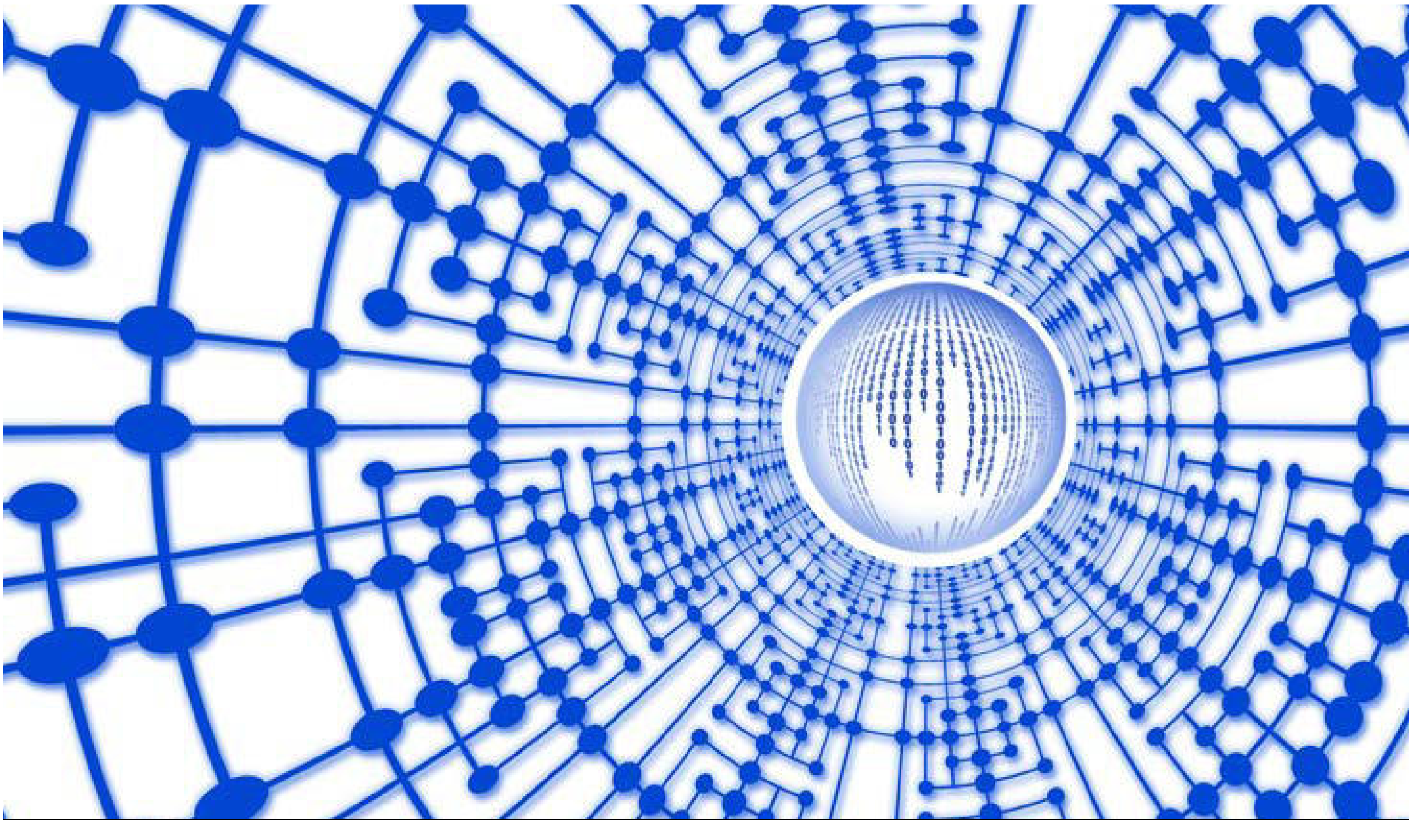
POLICY BRIEF

solutions



ESTABLISH DATA INFRASTRUCTURE TO COMPILE AND EXCHANGE ENVIRONMENTAL SCREENING DATA ON A EUROPEAN SCALE

ABSTRACT

Robust techniques based on liquid (LC) and gas chromatography (GC) coupled with high-resolution mass spectrometry (HR-MS) enable sensitive screening, identification, and (semi)quantification of thousands of substances in a single sample. Recent progress in computational sciences has enabled archiving and processing of HR-MS 'big data' at the routine level. As a result, community-based databases containing thousands of environmental pollutants are rapidly growing and large databases of substances with unique identifiers allowing for inter-comparison at the global scale have become available. A data-archiving infrastructure is proposed, allowing for retrospective screening of HR-MS data, which will help define the 'chemical universe' of organic substances and enable prioritisation of toxicants causing adverse environmental effects at the local, river basin, and national and European scale in support of the European water and chemicals management policy.

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CHALLENGE

Non-target screening (NTS) workflows are a powerful method for the large-scale analysis of environmental samples. They consist of wide-scope target, suspect, and non-target analysis. Recently, NTS has developed rapidly with the advance of HR-MS techniques, as reviewed elsewhere [1]. Smart monitoring combining cost-effective methods for wide-scope target and suspect screening with a battery of well-established high-throughput bioassays could be used routinely to reduce the risk of overlooking toxic chemicals in the environment [2, 3]. Continental scale wide-scope target and non-target screening required for an appropriate monitoring of complex chemical contamination is rapidly developing in many monitoring laboratories, as recommended in [4]. This will provide an amount of information unprecedented so far in environmental monitoring. Currently, monitoring data are typically stored and evaluated in a closed and decentralised way using non-harmonised formats and without substantial data exchange between the scientists and agencies involved. These deficiencies hamper the recognition of newly emerging contaminants and mixtures, the prioritisation and identification of the newly recognised chemicals, and the efficient exploitation of these data for quality assessment and management on a European and even global scale. So far, the infrastructure for storage, long-term archiving, open exchange, processing and analysis of these data is largely lacking, although the required technology for 'big data' repositories is already available [1, 5].

Any LC-HR-MS or GC-HR-MS technique needed for the detection of suspect and non-target chemicals generates large amounts of data, up to tens of GB per analysis. This brings environmental monitoring into the arena of 'big data'. Currently, only a fraction of the information from HR-MS measurements is extracted and the rest is discarded. The challenge is (i) to extract the minimum necessary information for a quick overview of presence/absence of a large number of suspects in the samples and (ii) to save all information from HR-MS (raw data) in a format harmonised at the European (and possibly global) level for retrospective screening of environmental samples for the currently known and future pollutants.

Dealing with tens of thousands of substances, their transformation products, technical mixtures, salts, isomers, etc. may lead to a great confusion when not coordinated. Neither the CAS No. nor the name is a sufficiently unique identifier for a compound of interest. At present, the US EPA CompTox Chemicals Dashboard (*https://comptox.epa.gov/dashboard*; > 875,000 chemicals, [6]) is uwsed as a reference for extracting quality checked information. Still, many of the chemicals with high production volumes and their transformation products are not found in this or any databases.

The identification of compounds with experimentally obtained mass spectra is more reliable than just exact mass matching of compound databases [7]. To ensure this, community-based databases containing measured mass spectra need to grow considerably. In addition, the mass spectra of 'unknowns' frequently recorded in environmental samples should be stored for future identification, as done in prototype form in the European (NORMAN) MassBank *(https://massb ank.eu/MassBank/)*. Complex mixtures of chemicals should be considered together with their complex effects and ecosystem impacts. Technical developments that now allow for recording extensive chemical fingerprints from NTS, toxicity profiles, and omics responses in laboratory test systems and wildlife and environmental DNA to address biodiversity are delivering enormous amounts of data. The challenge is to establish the infrastructure needed for data storage and the tools for multivariate biological and chemical analysis to facilitate the use of such data.

RECOMMENDATIONS

- Establish a federated European infrastructure storing raw non-target screening data converted into a common (open) format allowing for 'on demand' accessibility for retrospective screening
- Establish a central platform/database storing regularly updated information on available data sets Europe-wide and, eventually, at a global scale
- Establish a common European platform where the unique identifiers of newly discovered environmental pollutants can be shared in a harmonised format
- Apply commonly agreed workflow(s) for retrospective analysis to identify and prioritise pollutants frequently detected in environmental samples.

REQUIREMENTS

Establishing the data infrastructure for compilation and exchange of screening data on a European scale requires:

- Recognising the need for screening data within the framework of European water policy, air and soil pollution, and waste management
- Providing incentives by the European Commission to scientists, monitoring agencies, and Member States to share the screening data
- Providing incentives by the scientific journals to scientists to share the raw screening data in a harmonised format as a supplementary information to the publications using these data
- Securing European and national scale funding for establishment of the interoperable infrastructure
- Support of the European MassBank for systematic storage of mass spectral information of environmentally relevant substances *(https://massbank.eu/MassBank)*

- Further harmonisation of wide-scope target and suspect screening techniques in Europe
- Further development of HR-MS data processing workflows

ACHIEVEMENTS

SOLUTIONS/NORMAN DATABASE SYSTEM

The NORMAN network *(https://www.norman-network.net)*; a network of more than 80 reference laboratories, research centres and other organisations for monitoring of emerging environmental substances in Europe and North America; [8]) and the SOLUTIONS project *(https://www.solutions-project.eu)*; [9]) have pushed the limits of NTS further using European case studies. It is now possible to screen more than 2000 target compounds and more than 40,000 suspect substances in environmental samples. An online database for wide-scope target and non-target screening data was developed as a part of the NORMAN Database System *(https://www.norman-network.com/nds)* and the SOLUTIONS Database System *(https://www.norman-network.com/solutions/norman.php)*. The latter contains also a unique list of modelling-based prioritised substances, whose presence in the environment is not determined on actual occurrence measurements, but rather on the predictions related to their production volumes, use pattern, and how easy they can be released into environment.

NORMAN SUSPECT LIST EXCHANGE

A collaborative trial organised by the NORMAN network on a surface water sample from the Danube river basin revealed that suspect screening using specific lists of chemicals to find “known unknowns” was a very common and efficient way to expedite non-target screening [10]. As a result, the NORMAN Suspect List Exchange was founded *(https://www.norman-network.com/nds/SLE/)* and members were encouraged to submit their suspect lists. To date, more than 50 lists of highly varying substance numbers have been uploaded. Over 40,000 substances are available in the correspondingly merged SusDat database *(https://www.norman-network.com/nds/susdat)*. This database contains harmonised names, CAS Nos., SMILES, InChIKeys, “MS-ready structure forms” with chemical substances provided in the form observed by the mass spectrometer (e.g., desalted, as separate components of mixtures [11]), exact masses, retention indices, and modelling-based predicted ecotoxicity threshold values. Further > 40,000 substances are in the pipeline. The curation was done within the network using open-access cheminformatics toolkits. Starting in 2017, the NORMAN Suspect List Exchange and US EPA CompTox Chemicals Dashboard *(https://comptox.epa.gov/dashboard)* pooled resources in curating and uploading these lists to the Dashboard *(https://comptox.epa.gov/dashboard/chemical_lists).*

NORMAN DIGITAL SAMPLE FREEZING PLATFORM (DSFP)

A retrospective screening platform for hosting mass spectrometric data obtained by LC-HR-MS was created in 2017 *(https://norman-data.net)*, with the ambition of becoming a European and possibly global standard for retrospective suspect screening of environmental pollutants [5; Fig. 1]. This platform enables a quick and effective overview of the potential presence of thousands of substances either known or suspected to be present in the environment (based on the SusDat database), including a wide range of contaminants of emerging concern, their transformation products and unknowns, across a large number of samples and different matrices. A tool for semi-quantitative estimation of concentrations of any detected compound based on their structure similarity is being tested.

EUROPEAN (NORMAN) MASSBANK

A database for MS (mainly high resolution) spectra of substances of environmental and metabolomic relevance was created in Europe in 2011, using a format developed previously in Japan. European (NORMAN) MassBank *(https://massbank.eu/MassBank/)* now contains 57,472 unique mass spectra of 14,667 substances (accessed on 10 May 2019). The exact mass, fragmentation, and measurement information on all substances are feeding into the NORMAN DSFP. In SOLUTIONS, the joint efforts of the environmental and metabolomics community on Mass-Bank development improved and a developer consortium was founded *(https://github.com/MassBank/)*.

DEMONSTRATION AND EVALUATION IN CASE STUDIES

The databases developed within NORMAN/SOLUTIONS presented above have already been applied in several case studies related to SOLUTIONS. In the Joint Danube Survey 3 (2013; [12]), a wide-scope target and suspect screening using comprehensive substance lists was tested by several laboratories. Wide-scope target screening tools combined with bioassays were systematically used at the assessment of abatement options in the River Rhine catchment [13]. The NormaNEWS study was carried out in 2017, establishing a global emerging contaminant early warning network to rapidly assess the spatial and temporal distribution of contaminants of emerging concern in environmental samples through performing retrospective analysis on HR-MS data. The effectiveness of such a network was demonstrated through a pilot study, in which eight reference laboratories with available archived HR-MS data retrospectively screened data acquired from aqueous environmental samples collected in 14 countries on 3 different continents [14]. Wide-scope target (> 2100 substances) and suspect screening (NORMAN SusDat; > 40,000 substances) were performed in water, sediment, and biota samples in the Joint Black Sea Surveys (2016, 2017; [15]). A thorough analysis of waste water treatment plant effluents with a battery of SOLUTIONS/NORMAN bioassays was applied using wide-scope target and suspect screening in the Danube River Basin in 2017 in cooperation with the International Commission for the Protection of the Danube River (ICPDR) [16]. The outcomes of the case studies support further development of harmonised databases for archiving 'big data' from NTS.

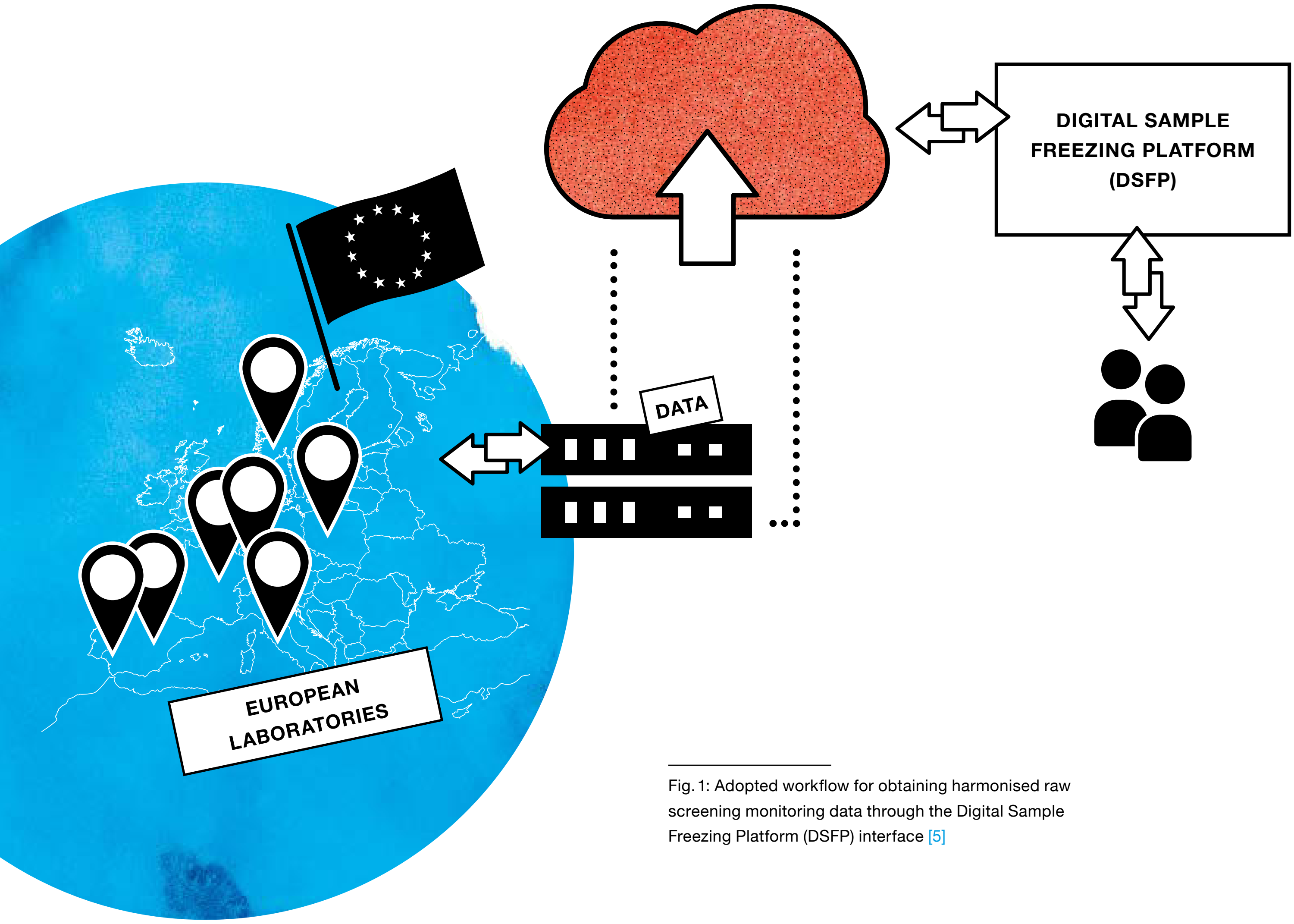

Fig. 1: Adopted workflow for obtaining harmonised raw screening monitoring data through the Digital Sample Freezing Platform (DSFP) interface [5]

SUPPLEMENTARY INFORMATION

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POLICY BRIEF

solutions

EXPLORING THE 'SOLUTION SPACE' IS KEY: EARLY-STAGE ASSESSMENT OF OPTIONS TO PROTECT AND RESTORE WATER QUALITY AGAINST CHEMICAL POLLUTION

ABSTRACT

Present evaluations of chemical pollution in European surface and groundwater bodies focus on problem description and chemical classification of water quality. Surprisingly, relatively low attention has been paid to solutions of chemical pollution problems when those are encountered. Based on evaluations of current practices and available approaches, we suggest that water quality protection, monitoring, assessment and management of chemical pollution can be improved by implementing an early-stage exploration of the 'solution space'. This follows from the innovative paradigm of solution-focused risk assessment, which was developed to improve the utility of risk assessments. The 'solution space' is defined as the set of potential activities that can be considered to protect or restore the water quality against hazards posed by chemical pollution. When using the paradigm, upfront exploration of solution options and selecting options that would be feasible given the local pollution context would result in comparative risk assessment outcomes. The comparative outcomes are useful for selecting optimal measures against chemical pollution for management prioritization and planning. It is recommended to apply the solution-focused risk assessment paradigm to improve the chemical pollution information for river basin management planning. To operationalize this, the present paper describes a still-growing database and strategy to find and select technical abatement and/or non-technical solution options for chemical pollution of surface waters. The solutions database and strategy can be applied to help prevent and reduce water quality problems.

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CHALLENGE

Water quality protection, monitoring, assessment and management is a key challenge, especially for chemical pollution [1–4]. Chemical pollution of surface water systems encompasses a group of distinct problems, characterized by highly diverse mixture compositions and associated high diversity of exposures and probable impacts [5, 6], in a context of widely varying non-chemical stressors and local natural conditions [7]. Consequently, there is a high diversity of protection and impact-driven restoration needs, which are the two key environmental objectives of the European Water Framework Directive (Article 4, WFD [1]). Water quality protection and assessment requires an improved coverage of this diversity to understand the water quality problems [6, 8–11] and also approaches to derive and select management solutions for those problems. This holds especially in view of the benefits of a non-toxic environment [12].

The EU-project SOLUTIONS (www.solut ions-proje ct.eu) aimed to address these problems. Due to the diversity of the mixture exposure, the idea of a 'onesize- fits-all' approach for protection and restoration is unlikely to be effective. To improve on the current situation, the project adopted a relatively novel risk assessment paradigm, solution-focused risk assessment [13].

This paradigm was proposed by the U.S. National Academy of Sciences after a wide-ranging evaluation of risk assessment practices of the U.S. EPA to improve the utility of risk assessments by an early-stage attention on the exploration of the 'solution space' for the environmental problem at hand. The 'solution space' is defined as the set of potential activities that can be considered to protect or restore the water quality against hazards posed by chemical pollution. The 'solution space' is wide. It not only concerns the option to implement a technical abatement option on a specific site as a reactive solution (e.g., an improved wastewater treatment installation), but also the strategic development and implementation of sustainable chemistry as a proactive solution [14]. A systematic database to store and retrieve options in the 'solution space' is lacking, but would be beneficial to water quality managers.

The solution-focused approach itself is not new, and its power has been established a long time ago. An early example is the successful reduction of the spread of cholera in nineteenth century London, by removing the handle of a drinking water pump [15]. The identified problem was thus an infectious disease, which was at that time thought to be spread via air. Data on the spread of the disease were collected and evaluated on a system-level basis (the disease incidences in a London neighborhood). By considering available information and solution opportunities, the implemented solution was a simple removal of the water pump handle. The WFD (Annex II) also stipulates that water quality managers collect available evidence on a water system-level basis (multiple lines of evidence), to establish the likelihood of stress factors to cause (potential) impacts and to subsequently derive effective programs of measures.

The current WFD-assessment and management cycle has been extensively described in guidances, be it that in the written texts and current practices the emphasis is on problem description and on water quality classification [16]. There is far less attention to the systematic translation of problems into management solutions (for protection or restoration).

The current assessment and management cycle follows the so-called DPSIR causal framework [8, 17]. This implies that water management practices consider the drivers of water quality reduction (D, e.g., economic activities), the resulting pressure (P, e.g., emissions of chemicals to the water system), the subsequent status of the water quality (S, e.g., the concentrations of compounds) and the resulting impacts (I, e.g., species abundance changes). Combining the information on D, P, S and I should yield the management response (R). The DPSIR approach explicitly suggests that the response R may consider potential solutions (the *Responses*, R) in the format of reductions of D, P, S and I. Water quality assessors are suggested to combine various lines of evidence (WFD-Annex II) to establish the *need* for water quality protection or restoration. It is a lost opportunity for water quality management not to support this step by organizing the systematic storage and retrieval of optional elements in the 'solution space', that is: the *'what can be done?'* question. As shown below, the solutionfocused paradigm can be aligned with the DPSIR cycle.

The provision of a database and strategy for exploring the 'solution space'—and optionally the experiences of others with specific solutions—would serve water quality management practices. The inclusion of a 'preference ladder' into such a system would further improve its usefulness.

Thus, the fundamental challenge of water quality management is to improve the utility of the solution-focused risk assessment paradigm, by providing a strategy for and information on the available options in the 'solution space', so that practitioners can select practicable options for their specific water quality problems. This challenge was addressed by improving the applicability of the solution- focused risk assessment approach for the problem of chemical pollution and by describing several case studies that show how that serves European water quality management. This was achieved utilizing the conceptual framework [18, 19] and adding new elements to it:

1. a database for technical abatement options and nontechnical solution options,
2. a strategy to use the solution-focused approach in practice and
3. chemical footprints (to enable evaluation of trends in chemical pollution threats and to predict approaches to handle future emerging pollutants).

RECOMMENDATIONS

- Implement the innovative paradigm of solutionfocused risk assessment [13] to water quality protection, assessment and management of European surface waters, in line with employing the DPSIR causal framework at all spatial scales (EU-wide, basin-specific and local water bodies).
- Pay early attention to the exploration of the ‘solution space’ that is available to *Respond* (the *“R”* in DPSIR) to chemical pollution threats.
- Collate technical abatement and non-technical solution strategies in a database and a strategy, to assist practitioners in identifying and selecting potential (cost-)effective options for preventing or solving chemical pollution problems.
- Combine the information on the ‘solution space’ with lines of evidence collated via the DPSIR approach and (cost-) effectivity to identify the optimum strategy.
- Apply sensitive indicators of chemical pollution (chemical screening, improved concentration-based and effect-based methods) to enable the evaluation of improvements in water quality (lowered chemical pollution stress and/or increased ecological status).
- Evaluate solution scenarios using all available lines of evidence, which not necessarily requires complete data on all aspects of pollution. This can be done *ex ante* to select the best options, and *ex post* to evaluate water quality improvement of an implemented management action.
- Employ rigorous operational monitoring to demonstrate that a solution scenario has been effective, and where extra efforts are needed
- Use comprehensive metrics, such as chemical footprints, to describe trends in water quality improvements following or expected from implementing a solution scenario. Chemical footprints can be used to evaluate options to evaluate strategies to handle future emerging pollutants

REQUIREMENTS

Developing effective solutions to water management challenges regarding the problem of chemical pollution requires:

- recognition that current risk assessments have limited utility, as they are often mainly problem oriented rather than solution focused, and are qualitative (binary classification of chemical pollutants) rather than quantitative (continuous ranking of chemical pollution severity);
- agreement that solution-focused risk assessment implies an improved utility of its outcomes for the derivation of management plans, due to an orientation to exploring the ‘solution space’ early on (provided that the problem remains to be comprehensively described);
- development and implementation of a sensitive indicator system for chemical pollution that shows water quality improvements that result from a set of measures taken, given that the current ‘one-out-all-out’ principle keeps positive trends invisible until the final goal is reached;
- incentives to operationalize the solution-focused risk assessment process by providing suitable guidance. This can be achieved either by adapting existing guidance documents from the series of *Common Implementation Strategy* documents (e.g., [16, 17]), or by providing novel documents; it will also be essential to provide tools for storage and retrieval of solutionoriented options and experiences;
- preventive evaluations of future emerging compounds, by modeling future chemical pressures resulting from actual and predictable developments in society;
- recognition that water quality assessors commonly combine multiple lines of evidence to establish the likelihood that chemical pollution affects water quality and to subsequently derive programs of measures;
- the active use, evaluation and further improvement of the solution-focused risk assessment approach.

ACHIEVEMENTS

1. THE DPSIR CAUSAL APPROACH, THE CONCEPTUAL FRAMEWORK AND THE RESPONSE ISSUE

The WFD [1] is based on a water systems-level approach, recognizing that water systems are natural systems of river basins that commonly cross multiple national borders and jurisdictions. Water systems may be threatened by the mixtures of chemicals (‘specific pollutants’) that are emitted in significant amounts to the water system. Those result in a highly diverse chemical pollution pattern at the site of emission and/or downstream [6, 9].

To handle this vast diversity of pollution situations, we suggest that water quality assessors employ a systematic approach to diagnose water quality problems and their probable causes, as prescribed in the WFD-Annex II. We therefore combined the WFD-suggested DPSIR approach [8, 16]) with the extended conceptual framework for solution-focused management of chemical pollution in European waters [13, 19]. The result of the combined concepts is shown in Fig. 1. The present paper focuses specifically on early-stage attention for exploring optional *Responses* (R), that is, to explore the ‘solution space’ when a water quality problem is hypothesized or found. The WFD (Annex VI) does provide already a list of standard measures that can be addressed as potential solutions to be considered for the programs of measures (Additional file 1). The list suggests that the ‘solution space’ is large, but it does not provide a very specific or operational strategy or solution approaches. Figure 1 suggest that the ‘solution space’ encompasses technical abatement options (lower left, 'Abatement'), but also suggests how to explore the 'solution space' further (via the entries 'Chemicals', 'Environment' and 'Society'), as detailed below.

Given the conceptual framework of Fig. 1 and the tools and services to characterize water quality problems [20], we aimed to systematically collate abatement techniques and management options and strategies and to make the results available for re-use by others encountering a similar chemical pollution problem. Systematic storage of those—with or without evaluating them—enables a whole community of users to retrieve collated options and experiences, and thus to explore a wide array of options. Users can retrieve options in the 'solution space', to derive programs of measures for their specific problem (see below).

As compared to current practices, the combined framework (Fig. 1) encompasses a change from single chemicals per site to a system-level approach, from a problem description-oriented approach to (also) a solution-targeted approach, and from a limited view on the 'solution space' to a systematic basis to recognize that the 'solution space' is large.

2. THE EARLY EXPLORATION OF THE 'SOLUTION SPACE

The early management attention to the *Response*-step (R) of the DPSIR causal cycle can be supported by systematic collations of data on technical abatement options and a description of the management strategy. To that end, such information was collated in a database of technical abatement options [21], and in a proposal for the systematic evaluation of non-technical solution scenarios (see Additional file 1). Both were designed to be broadly applicable. This supports users in exploring the 'solution space' and may help to inspire them to evaluate options they would never have thought of, and the availability of a database of options helps to avoid that 'the wheel is reinvented over and over again'.

The *technical options* are provided as a database of technical abatement options and efficiencies for the application in wastewater and drinking water treatment plant construction and upgrading [21]. The database provides insights into the degree of expected removal of hazardous chemicals from wastewater and raw water for drinking water production for various techniques. This was achieved by an analysis of the installation-specific removal efficiencies of chemicals with different physical–chemical properties. It should be acknowledged that the database can be continuously expanded, based on the experiences gained, which would further improve the value of the technical abatement database.

The *non-technical options* were found to be highly diverse (Fig. 2). The exploration of prevention and management strategies is currently formatted as a strategy to explore the 'solution space' (Fig. 2). Note that this figure is directly derived from and related to the conceptual framework (Fig. 1). It provides a generic scheme that supports end users in exploring the non-technical 'solution space'. The visualization of the 'solution space' in Fig. 2 shows that there are three general levels to approach a pollution problem, going from operational via tactical to strategic options. Note that the discrimination between these levels is not strict. Further details are in Additional file 1. Figure 2 shows how the conceptual framework (Chemicals, Environment, Abatement and Society, Fig. 1) thus in general supports a systematic exploration of the available 'solution space' (Fig. 2).

The application of the strategy and the scheme of Fig. 2 are further elaborated in Additional file 1. There are two final remarks on the 'solution space' in relation to other (non-chemical pollution) stress. First, it should be noted that the exploration of the 'solution space' in the present paper focused on chemical pollution only. However, the diagnosis of impacts of all stressors may show that chemical pollution is only part of the problem, or even negligible, and that the 'solution space' for the integrated management plan should also consider the solutions to other stressors. Second, it should be noted that a single solution strategy may help reduce the impacts of multiple sources of stress. For example, zonation (between land use and water systems) helps reduce emissions of both nutrients and agricultural chemicals.

3. PRIORITIZING THE INTENSITY OF MEASURES AGAINST CHEMICAL POLLUTION

Diagnostic results—ranking sites and compounds regarding the relative importance of chemical pollution to cause harm—are needed as a first step to help prioritize the need for and intensity of the measures that can be taken to prevent or reduce chemical pollution problems. As any compound (currently in trade, or produced in the future) can pose harm (alone or in a mixture), the WFD and current research therefore consider all compounds and their mixtures. The diagnostic step is supported by diagnostic tools and services (e.g., [6, 10, 11]) and helps to steer management efforts to those sites and compounds that are most problematic for reaching the WFD environmental goals (good chemical and ecological status). The exploration of the 'solution space' might focus on prioritized water bodies and compounds, but would also consider lowerranked cases where a solution option is relatively easy to implement.

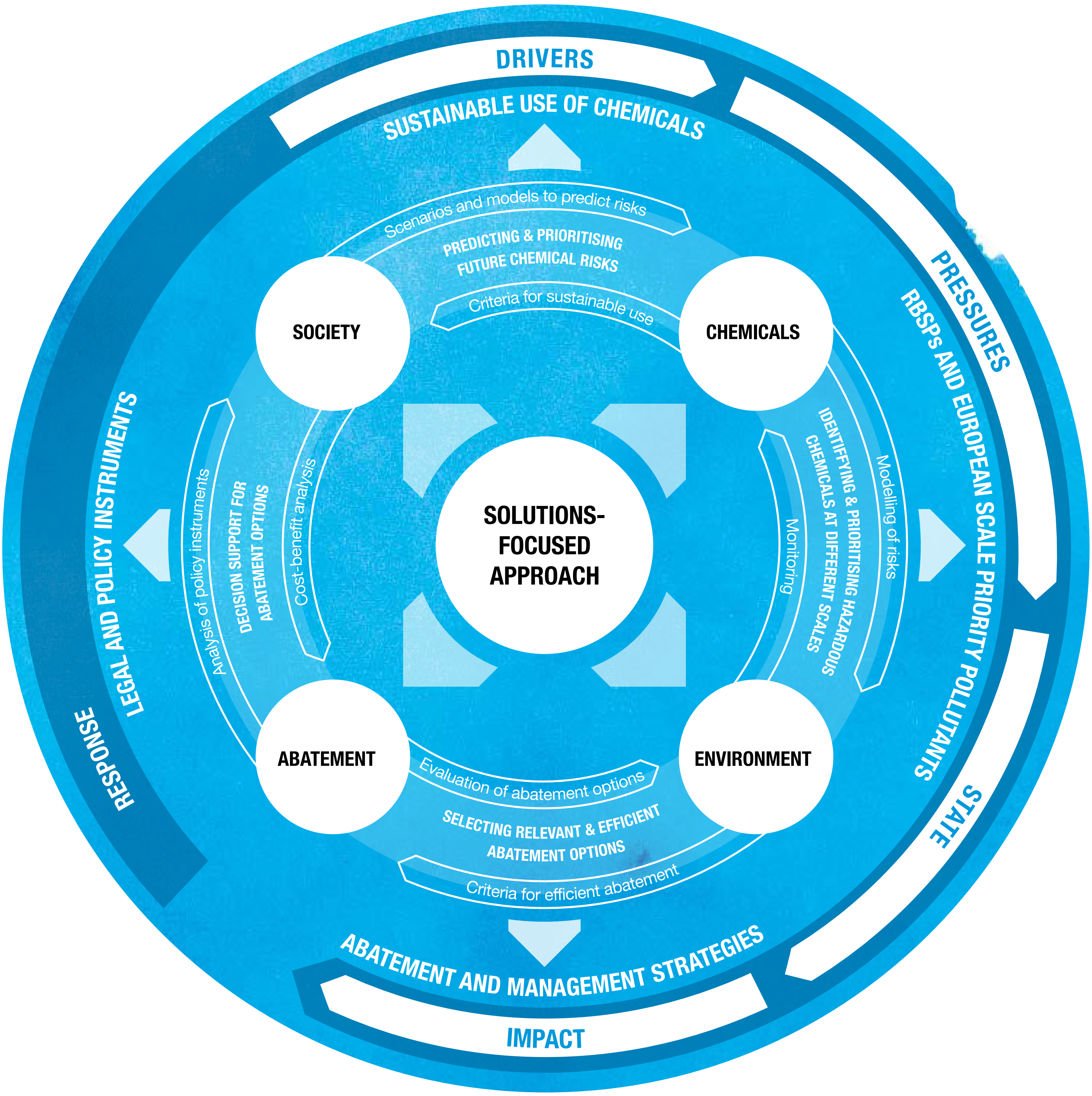
Fig. 1: The solution-focused risk assessment paradigm as proposed by the U.S. National Academy of Sciences [13] was operationalized for the assessment and management of chemical pollution of surface waters [19]. This supports practitioners in considering the 'solution space' for preventing or reducing chemical pollution (including technical abatement options), which can be valued as potential Response to pollution

4. SOLUTION-FOCUSED PRACTICES

So far, the recommended approaches are introduced as novel concepts, with generic schemes to assist water quality assessors in practice. The combination of the solution-focused framework, the diagnostic approaches and the database and strategy for exploring the ‘solution space’ yields a novel flow diagram (Fig. 3). The diagram closely relates to the current WFD-assessment and management cycle, but emphasizes the novel key step (early focus on exploring the ‘solution space’) as well as the aforementioned recommendations to improve current practices (such as to follow the systems-level approach of the WFD).

5. EVIDENCE FOR IMPROVED STATUS

solution strategies resulted in reduced chemical pollution problems in European surface water systems.



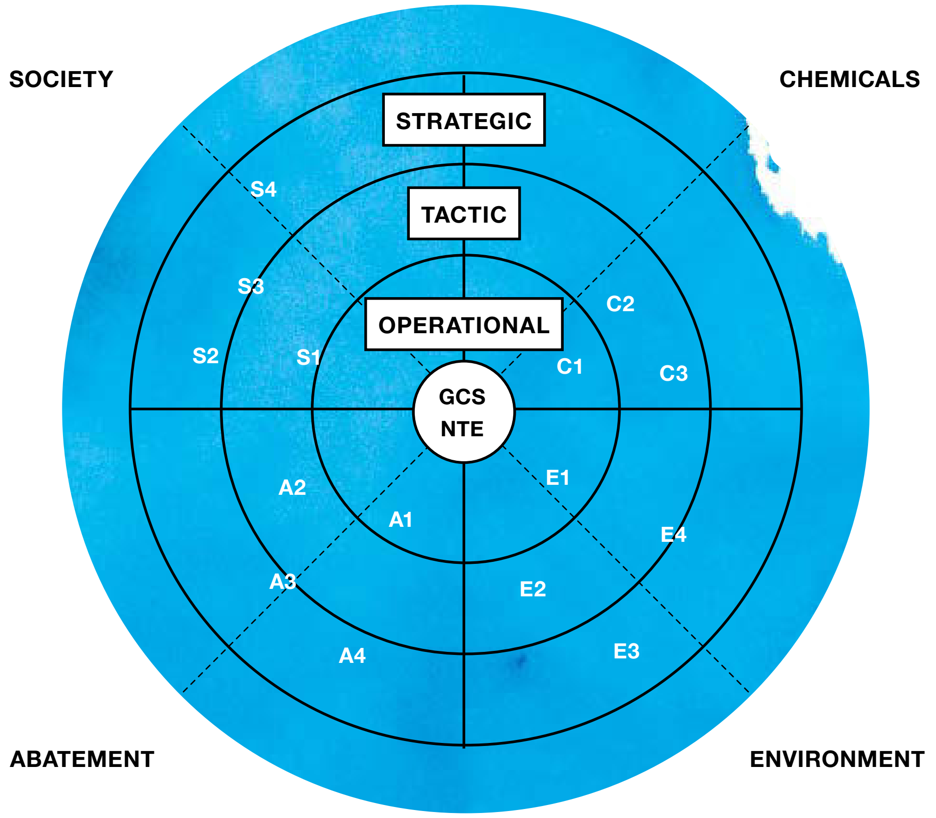


Fig. 2: The strategy for exploring the 'solution space', based on the conceptual framework (Fig. 1, [19]). The different codes (C1, C2, … etc.) visualize that there are widely different options in the 'solution space', ranging from operational options for local application (e.g., to swiftly solve a local water quality problem), up till tactical and strategic options for (inter)national water governance. The diversity of codes is explained in the text, and some examples are summarized in Additional file 1

First, the chemical, bioanalytical and ecological tools that are available were used to evaluate chemical pollution in relation to the efficacy of wastewater treatment plants (WWTPs) in removal of chemicals and reducing risks and impacts [22, 23]. The evaluation considered WWTP upgrades with an added activated carbon treatment step and considered up- and downstream and before/after comparisons. It was demonstrated that the improved treatment influenced ecosystem exposure (reduced) and quality (improved). The extra carbon treatment was beneficial for the chemical, biological and ecological status of the receiving water bodies [22–25].
Second, additional studies considered ten riverbank filtration sites along the River Rhine and its tributaries, and looked at modeling, existing data and additional analytical measurements of trace organic compounds to assess the attenuation potential of selected chemicals present in the surface water by riverbank filtration. For a site with long retention times to the drinking water well, the results enabled the categorization into very persistent, partially removable and fully removable compounds in the given time scales [26]. For three sites with short travel times, a broad analytical screening enabled categorization of the chemicals into "persistent" and "naturally attenuated" classes [27]. For one Dutch site, the efficiency of anaerobic riverbank filtration was assessed before and after reverse osmosis treatment, using a battery of bioassays combined with non-target screening. The treatment process of reverse osmosis was characterized in more detail using spiked anaerobic riverbank filtrate [28].
Monitoring can also directly trigger a solution strategy or method. Daily wide-scope target and non-target screening of water samples using high-resolution mass spectrometry at River Rhine stations triggered successful abatement measures when non-regulated and nonmonitored relevant chemicals were detected [29]. Many pollution sources can be located in river catchments via DPSIR analyses and/or monitoring. The example case studies cited above, as well

as scenario studies with models [6], show that corrective measures, such as change in industrial production processes or improved waste management, can significantly reduce or eliminate discharges and chemical pollution risks.

6. EXPLORING FUTURE OPTIONS

The compilation of optional technical abatement and management strategies can be followed by a ‘fitness check’ of expected water quality improvements. Here, the water quality assessor evaluates each option with respect to critical aspects, such as practical implementation, costs and efficacy. Scenario analyses can be run to evaluate the expected improvements in water quality, applying component-based approaches. An example result of such a comparative assessment is shown in a case study of future emission scenarios of chemicals at the European scale under alternative policy strategies [6, 30]. The most remarkable result was a highly positive effect (35 % less toxic pressure, expressed as multi-substance potentially affected fraction, msPAF) of the phasing out of 26 substances of very high concern (SVHC) listed on the REACH Candidate List (out of the 1357 chemicals registered under REACH that were included in the ‘future management’ scenario). This clearly shows the high potential of focused regulatory measures to reduce the total chemical burden in general [31]. But specifically, the water quality change in relation to SVHC-focused emission reduction measures appeared to be more than proportional, driven by non-linear exposure–effect relationships (see also [32, 33])

7. EVALUATION AND COMMUNICATION OF TRENDS: CHEMICAL FOOTPRINTS

Communicating the output of the changes following from an implemented solution scenario and/or future management scenarios requires an innovative approach for evaluating trends and communicating results. This is key, given the diverse appearances of the chemical pollution problem. A chemical footprint approach was developed for this, providing summary information of the chemical pollution for an area [34, 35]. The chemical footprint indicator provides summary insights in the net likelihood of chemical pollution to cause harm. Indications for a decreasing chemical footprint were found in a retrospective study of a European basin [35], in line with emission reduction policy objectives and efforts and associated observations made with effect-based methods.

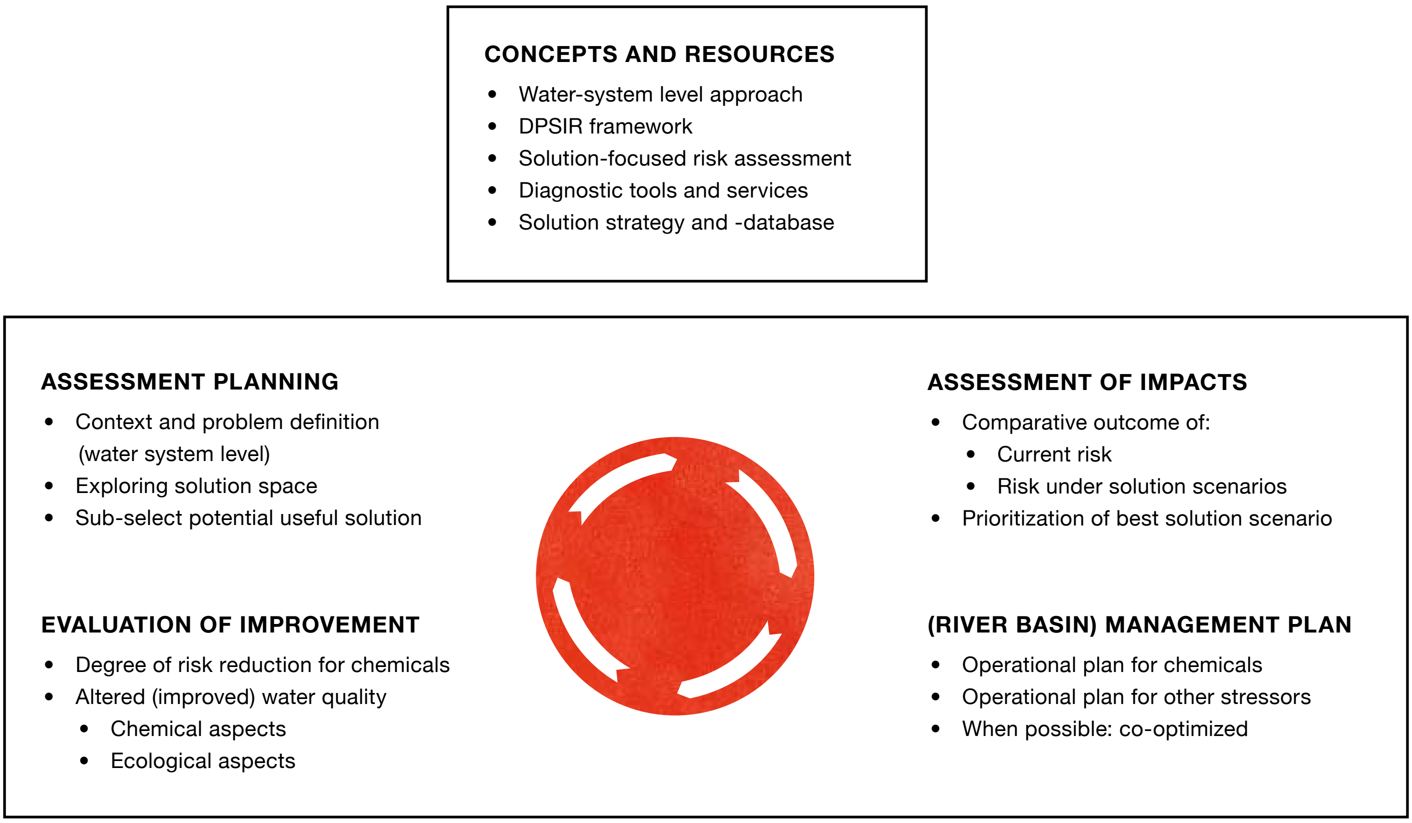


Fig. 3: Concepts and resources for solution-focused risk assessment (top) and the flow diagram for solution-focused risk assessment of chemical pollution of surface waters

The chemical footprint indicator can currently provide insights in the chemical footprint at the level of local water bodies. That is, the management-relevant outcomes of current chemical footprint analysis consist of (1) information whether and in how far upstream 'source' areas contribute to a local mixture risk, (2) information on the relative importance of chemical emissions to the local mixture toxicity and (3) information on whether and in how far mixture toxicity from a polluted water body is transported to downstream 'target' areas [36]. These types of information are key to define programs of measures against pollution and which actors to address (upstream or local) who have shared responsibility in causing risks (1 and 2) and to inform water managers of the downstream areas.

8. FURTHER DEVELOPMENTS

The success of water quality protection and management regarding chemical pollution depends on the possibility to identify and implement optimal abatement techniques and management approaches [31, 37]. The implementation of the solution-focused risk assessment paradigm into the practice of European water management is supported by a conceptual framework that guides the assessment process and provides a systematic overview of available abatement and management strategies. The abatement database and the management strategies are continuously expanding, following the continued cycle of water quality management activities

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at *https://doi.org/10.1186/s12302-019-0253-6*.

Additional file 1.
Strategy to explore the 'solution space' to protect and restore water quality in relation to chemical pollution.

Abbreviations
DPSIR: Drivers, Pressure, Status, Impact and Response; msPAF: multi-substance potentially affected fraction; REACH: registration, evaluation, authorization and restriction of chemicals; SVHC: substances of very high concern; WFD: Water Framework Directive; WWTP: wastewater treatment plant.

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POLICY BRIEF

MIXTURES OF CHEMICALS ARE IMPORTANT DRIVERS OF IMPACTS ON ECOLOGICAL STATUS IN EUROPEAN SURFACE WATERS

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.

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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:

1. 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 neither 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 lessthan- good ecological status (cf. WFD-Annex II).

RECOMMENDATIONS

- ImplemImplement 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 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/)* and the IPChem database (https ://ipche m.jrc.ec.europ a.eu/RDSId iscov ery/ipche m/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 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.

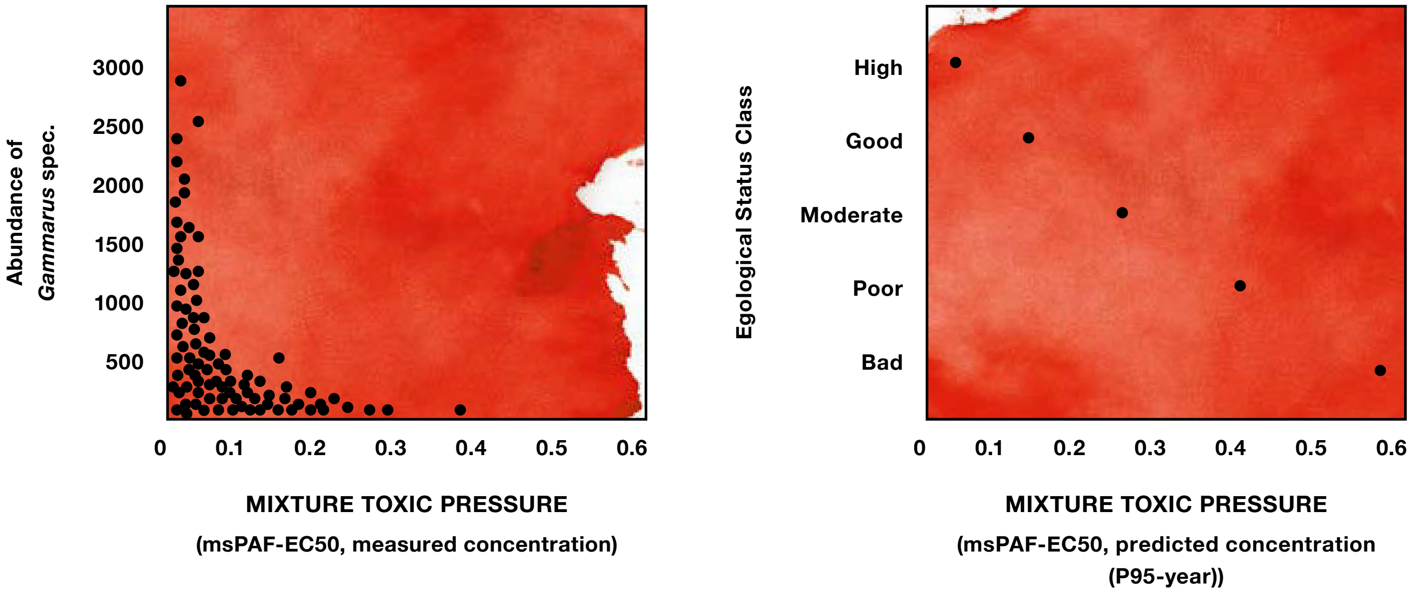

Fig. 1: Evidence for chemical mixtures being a limiting factor for two impact endpoints. Left: area: Dutch surface waters; *X*-values derived from measured concentrations of chemicals in the Netherlands; *Y*-values are abundance data for an example taxon; dots: raw *XY*-data (nearly 6000 sites). Right: 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)

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 effectbased 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 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.

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at *https ://doi.org/10.1186/s12302-019-0247-4*.

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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POLICY BRIEF

A HOLISTIC APPROACH IS KEY TO PROTECT WATER QUALITY AND MONITOR, ASSESS AND MANAGE CHEMICAL POLLUTION OF EUROPEAN SURFACE WATERS

ABSTRACT

Chemical pollution of surface waters is a societal concern around the globe. Key problems in current water quality protection, assessment and management are the narrow focus on a small fraction of the chemicals in commerce, concerns for increasingly diverse chemical emissions, and lack of effective diagnosis and management approaches. In reply, three key concepts to address these challenges were developed and tested. The approaches were developed in the context of the European Union Water Framework Directive, based on principles such as the DPSIR-causal framework (Drivers, Pressure, Status, Impact and Response) and the basic feature that water protection and management should be based on a water-system level approach.

Collaborative actions of researchers and stakeholders resulted in: (1) an operationalization and implementation of the solution-focused risk assessment paradigm as proposed in 2009, to improve the utility of risk assessments, (2) the provision of a large set of tools and services to prevent, monitor, assess and manage complex mixture pollution problems, and (3) a strategy and a database on intervention options. These three elements were recognized as core elements to help protecting and improving water quality. Although the methods were developed in the context of water quality problems in Europe, the three elements can be applied globally in water quality protection and management.

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CHALLENGE

Chemical pollution of surface waters is a societal concern around the globe [1–3]. Key problems in current water quality protection, assessment and management can be identified as a too narrow focus on a small fraction of the chemicals in commerce, concerns for increasingly diverse chemical emissions, and lack of effective diagnosis and management approaches [4] (see Additional file 1). The present paper is a Policy Brief that considers three overarching concepts to address these challenges. It is based on a broad evaluation of the results the EU-Integrated Project "SOLUTIONS" *(http://www.solut ions-proje ct.eu)*. Other Policy Briefs from this project published in the present journal provide further information on specific subjects. The research specifically considered the problem of chemical pollution of surface waters in Europe [5], being evaluated in the context of the European regulation (the EU-Water Framework Directive [6]). Despite this, the results can be applied globally in water quality protection and management.

Considering chemical pollution, the Water Framework Directive (WFD) defines 'pollution' (Article 2.33) as the human-caused introduction of substances into the air, water or land which may be harmful to human health or the quality of aquatic ecosystems, including the services provided to humanity by water resources of good quality. Water quality protection, assessment and management is faced with an extremely complex problem, given the more than 145,000 chemicals registered in the EU Classification and Labeling Inventory of New and Existing substances in the EU, and the rising chemical diversity and production masses [7–9]. Water quality can, thus, be threatened by an infinite number of local, specific mixtures of these. Global strategies to prevent and limit chemical pollution threats focus on products (improve chemical safety), emissions (limit) and the receiving environment (reduce mixture exposures). EU-Regulations and Directives such as REACH [10] and the WFD [6] have been cited as global examples of modern, comprehensive regulatory approaches [11]. Although the WFD was published in 2000, a good water quality status was not yet reached in 2012 and 2018 in a large fraction of Europe's surface waters [5, 12]. Chemical pollution poses a lasting and diversifying problem to surface water quality [7], together with the aforementioned other stressors [13].

In this Policy Brief, we address four major challenges: (1) to respond to the currently observed issue of insufficient chemical and ecological status, (2) to develop a holistic view on assessing and managing chemical pollution of complex mixtures, (3) to operationalize that view in the formats of a conceptual framework for protection, assessment and management of complex mixtures and associated tools and services, and (4) to address the problem that the wide diversity of mixture problems asks for an intervention measures database and -strategy that can be used to identify abatement options and select the best approach to solving the diversity of pollution problems. The overall challenge was to characterize chemical pollution in a comprehensive way with limited resources, such that the likelihood of impact of chemical pollution can be diagnosed, that risks to ecosystems and human health and resources for drinking water production can be prevented and limited at minimal treatment costs, and that optimized programs of measures can be derived.

RECOMMENDATIONS

- Start addressing chemical pollution problems from a holistic, water-system level viewpoint.
- Consider that any water body can be exposed to a unique set of specific pollutants, beyond the obligatory priority substances (PS) and the river basin-specific pollutants (RBSP), which act as mixture.
- Utilize the SOLUTIONS conceptual framework and intervention database and -strategy to assist water quality assessment practices in diagnosing mixture problems and to select measures that optimally prevent and reduce impacts of chemical pollution.
- Apply the set of SOLUTIONS tools and services for the so-called *Analysis of Impacts*-step that is described in the WFD-Annex II, to diagnose the likelihood that chemical pollution threatens water quality of a water body.
- Support the application of the aforementioned tools and services by expanding the current guidance and by establishing communities of practice.

REQUIREMENTS

Implementing a holistic approach to assess and manage chemical pollution of European surface waters requires:

- Recognition that chemical pollution problems need to be assessed and managed in a holistic way, covering all substances and their mixtures:
  - Consider priority substances (European scale).
  - Consider river basin-specific pollutants (basin
  - scale).
  - Consider sub-basin and local pollution (see [14]).
- Recognition that mixture exposures and potential effects are common.
- Recognition that current per-chemical assessments provide too limited information for comprehensive impact assessment and derivation of programs of measures to reduce chemical pollution.
- Development of, and agreement on, a set of diagnostic approaches with which water quality assessors can be

assisted in determining pollution hot spots and priority pollutants and -mixtures, to help formulating and focusing programs of measures to the sites and compounds mattering most.
- Development and implementation of a user-oriented decision tree with which the optimal diagnostic approach can be derived for the specific context of a water quality problem.
- Development of effective methods to communicate the results of chemical pollution assessments, such that water quality experts can interpret and handle the results of the diagnostic approaches in their daily practice.
- Adoption and expansion of the intervention database and -strategy, to enable water quality managers to explore the optional solutions for the water quality problem, given the results of the diagnosis.

ACHIEVEMENTS

OVERVIEW

The research addressed the main goals of the European Innovation Partnership for chemical pollution of Europe's water systems [4] (compare Additional file 1: Material) and achieved to provide:

1. A conceptual framework for the protection, monitoring, assessment and management of chemical pollution in European surface waters.
2. A wide array of methods with which water managers can diagnose whether, where, and due to which compounds chemical pollution poses threats to water quality.
3. A strategy for and an overview of potential measures, to provide water quality professionals with insights in the 'solution space' to reduce the water pollution problems, and thus to support deriving (cost)effective programs of measures.

All three achievements were developed with an eye on the holistic principle on which the WFD is based. This contrasts to the current practices in chemical pollution assessments, which have evolved into approaches that often focus on individual chemical measurements, with neglect of the water system context [15]. The diagnostic methods were developed because the current guidance is very limited in this respect (see WFD-Annex II text [6], and [14]). The attention was focused on intervention measures because current approaches are often focusing on describing the problem rather than on (also) providing solutions that can be implemented to improve water quality. Other closely related achievements, describing, e.g., the wide array of specific diagnostic methods, are presented in other Policy Briefs of the SOLUTIONS project.

THE CONCEPTUAL FRAMEWORK

The WFD assessment and management cycle is based on the DPSIR-causal framework. This consists of a systematic analysis of the Driving forces (D), the resulting Pressures on the environment (P), the Status characteristics of the water bodies (S), and finally the impact to water quality (I), which triggers a management Response (R) to protect or restore water quality [14].

In line with the DPSIR-cycle and combining that with the solution-focused risk assessment paradigm [16], a conceptual framework was developed for the protection, monitoring, diagnostic assessment and management of chemical pollution problems. The solution-focused risk assessment paradigm was proposed to improve the utility of chemical and environmental risk assessments [16]. This paradigm was operationalized, resulting in the comprehensive solution-focused framework shown in Fig. 1.

The figure shows four 'corner-stone' elements, their mutual relationships and the management-relevant outputs that are generated when the framework is applied. The outer ring shows that and how—in principle— chemical pollution can be reduced, such as (top) via the sustainable use of chemicals. In essence, the conceptual framework describes the transfer from a *problem-oriented* approach ('what is the risk') to the realm of the *solutions-focused* outcomes ('what can be done if there is a risk or an effect'). The diagnostic tools and services (provided by the RiBaTox tool, see below) were designed for the key elements of the conceptual framework. The intervention database and -strategy (for technical and non-technical abatement options) was a specific product, positioned separately (lower left) in the framework.

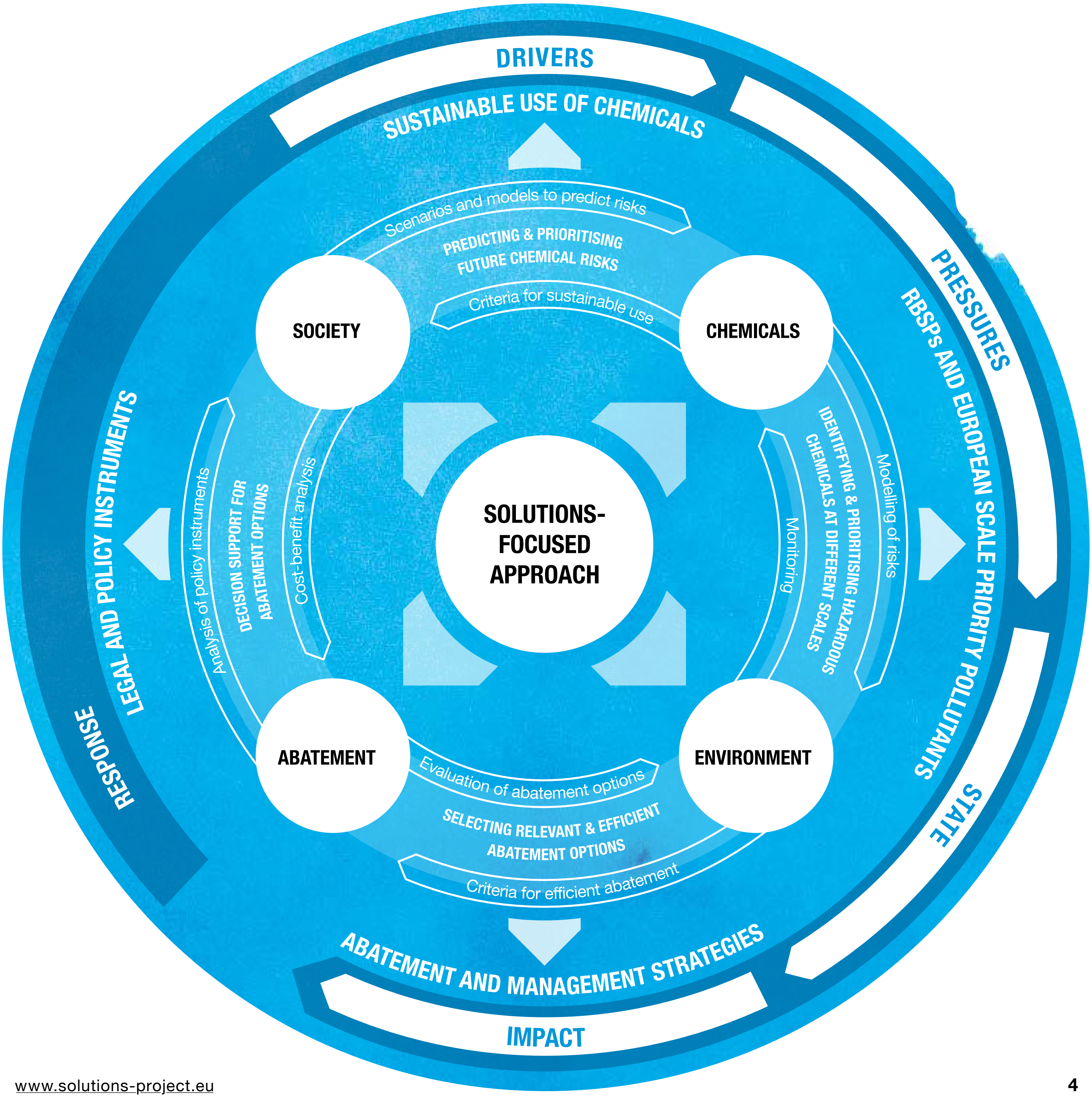
VERSATILE TOOLS AND SERVICES

The research provided a variety of tools and services to assist in the process of assessing the likelihood that chemical pollution threatens water quality (cf. WFDAnnex II). This is referred to as 'diagnosis' in this paper. The diagnostic methods are summarized and characterized in the other SOLUTIONS Policy Briefs. For example, methods can be selected for early-stage exploratory assessments on the presence of chemicals [19], via refined component- and effect-based diagnostic approaches of impacts [20, 21] to specific biological quality elements [22] and the ecological status [13], up till integrated modeling [23]. The methods cover the full array of the DPSIR-causal approach (Fig. 1). An assessor can derive the likelihood of chemical pollution to pose harm by combining the information from integrated modeling of expected threats associated to societal activities (Drivers), via wide-ranging non-target screening results on the presence of chemicals up to information gained by targeted component- and effect-based diagnostic and monitoring methods. The assessor can select the tools and services that are relevant to their local problem definition, using the decision tree approach of the RiBaTox-webtool *(https://solutions.marvin.vito.be/)*. If needed, the methods can be applied in a tiered way.

THE INTERVENTION DATABASE AND -STRATEGY

The research resulted in an intervention database and -strategy to help assessors to solve chemical pollution problems [18]. The strategy to identify options to derive programs of measures and thus to explore the 'solution space' is a key part of the conceptual framework (Fig. 1), and stresses the idea of paying early attention for the Response-step of the DPSIR-cycle.

The 'solution space' has been identified as large. That is, solutions can vary widely, ranging for example from operational changes in the technical designs of a waste water treatment plant facility up to strategic improvements in the design of chemicals ('safe by design'). Measures can also be non-technical, such as via 'zonation' between the land use that causes the emissions of compounds and the water bodies. The overview of technical and nontechnical abatement strategies provides end-users with a practical but not



limiting basis for derivation of (cost-) effective management plans. Users can select the options that could apply to their pollution problem. Integrated modeling [23] can be used not only to explore threats of current emissions, but also to evaluate future emission scenarios and the effects of abatement measures.
It is recommended to apply intervention tools and -strategies in the earliest stages of a WFD DPSIR-cycle. Various risk prevention and management solutions may be simple to implement and of a *no regret* kind.

UTILITY OF THE ACHIEVEMENTS

Recommended methods should have practical utility [4]. Therefore, the achievements were tested and evaluated in case studies, with intensive contacts with the stakeholders. In their final evaluation of the project, the stakeholders expressed their positive attitude to the three main elements of the holistic and comprehensive set of approaches to prevent, monitor, assess and manage chemical pollution of European surface waters [24]. They recognized the value and utility of the comprehensive principles (the conceptual model and the intervention database and -strategy). They also valued the large set of versatile tools to address the problem of complex mixtures in aquatic ecosystems. The utility relates not only to tools and services, but also to the wide array of chemicals and mixtures that can be identified, and of which the likely impacts can be characterized [19, 21]. The number of chemicals for which diagnostic solution-focused assessments can be made is vastly expanded as compared to the current number, of approx. 300 compounds considered separately [25], whilst including their mixtures.

Fig. 1 (left): The SOLUTIONS conceptual framework (center) [17] is an overlay of the DPSIR-causal framework [14] (outer circle) and the solution-focused risk assessment paradigm [16]. DPSIR's "R" closely relates to the solution-focused approach, and shows opportunities to protect and limit pollution via all management options [18]. The 3rd WFD-management cycle (planned for 2022–2027) can define Responses based on the outcomes of monitoring data and other insights gained from the 2nd DPSIR-cycle (2016–2021)

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at *https://doi.org/10.1186/s12302-019-0243-8*.

Additional file 1.
Research requirements formulated under the European InnovationPartnership (2010).

Abbreviations
DPSIR: Drivers, Pressure, Status, Impact and Response; PS: priority substance; REACH: Registration, Evaluation, Authorisation and Restriction of chemicals; RBSP: river basin-specific pollutant; WFD: Water Framework Directive.

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Availability of data and materials
Research requirements formulated under the European Innovation Partnership (2010) are available under Additional file 1: Material.

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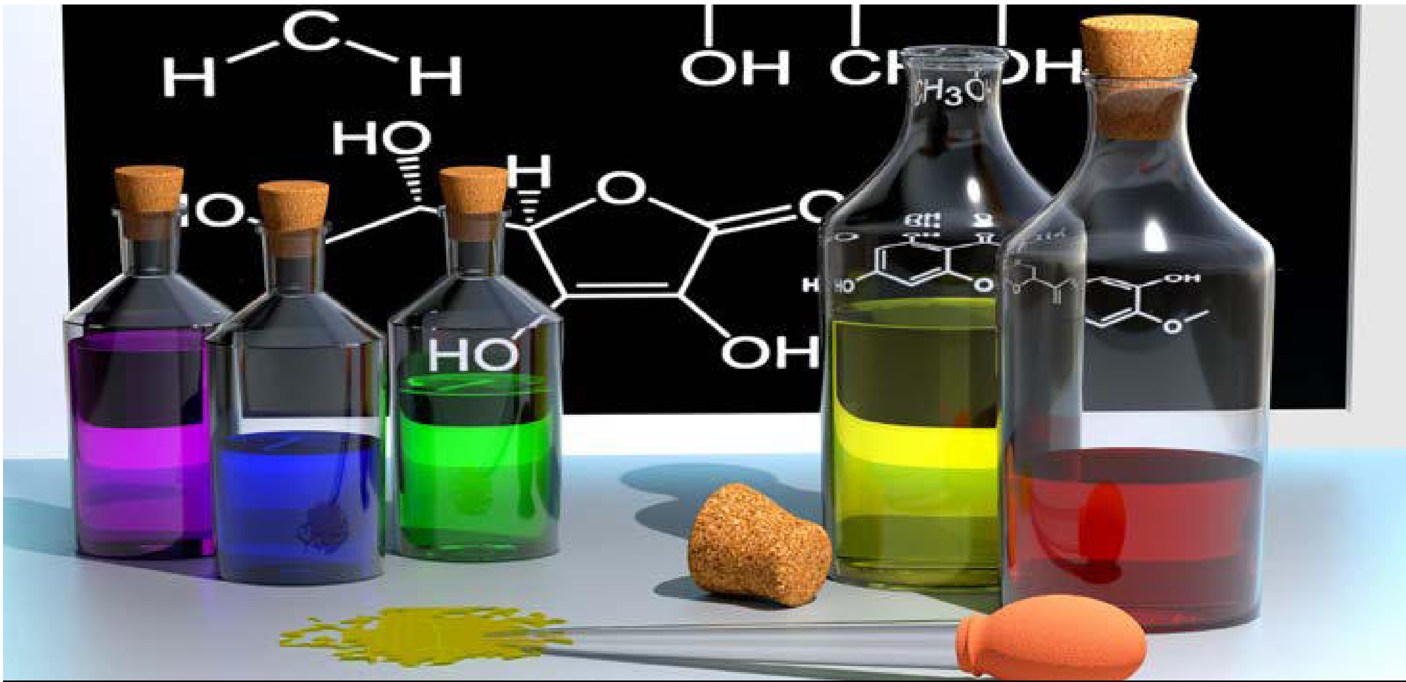
POLICY BRIEF

solutions



IMPROVED COMPONENT-BASED METHODS FOR MIXTURE RISK ASSESSMENT ARE KEY TO CHARACTERIZE COMPLEX CHEMICAL POLLUTION IN SURFACE WATERS

ABSTRACT

The present monitoring and assessment of water quality problems fails to characterize the likelihood that complex mixtures of chemicals affect water quality. The European collaborative project SOLUTIONS suggests that this likelihood can be estimated, amongst other methods, with improved component-based methods (CBMs). Various CBMs are described and illustrated, often representing improvements of well-established methods. Given the goals of the WFD and expanding on current guidance for risk assessment, these improved CBMs can be applied to predicted or monitored concentrations of chemical pollutants to provide information for management planning. As shown in various examples, the outcomes of the improved CBMs allow for the evaluation of the current likelihood of impacts, of alternative abatement scenarios as well as the expected consequences of future pollution scenarios. The outputs of the improved CBMs are useful to underpin programmes of measures to protect and improve water quality. The combination of CBMs with effect-based methods (EBMs) might be especially powerful to identify as yet underinvestigated emerging pollutants and their importance in a mixture toxicity context. The present paper has been designed as one in a series of policy briefs to support decisions on water quality protection, monitoring, assessment and management under the European Water Framework Directive (WFD).

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CHALLENGE

Good water quality is vital for human health and ecosystems. Unfortunately, recent reports show that large numbers of European surface water bodies do not achieve a good status (e.g. [1–5]). Especially the concerns about chemical pollution and observations of an insufficient ecological status of many water bodies trigger the need for better assessments, protective action against chemical pollution and restoration measures.

The current assessment of chemical pollution under the European Water Framework Directive (WFD, [6]) is insufficient, given that only very few (0.2 %) of the more than 145,000 commercially relevant and potentially emitted chemicals are considered in water monitoring and management efforts [2, 7, 8]. Of course, chemicaloriented regulations (such as REACH, [9]) provide an approach to prospectively assess chemical safety, with a fairly comprehensive coverage of the chemicals in trade, but that does not ascertain that water quality is always fully protected everywhere for all those chemicals. These prospective assessments are based on predicted environmental concentrations combined with component- based methods (CBM) for effect assessment. On a European scale, monitoring and management of surface water quality have so far largely focused on per-chemical evaluations of 45 priority substances (PS) of Europe-wide concern, while approximately 300 chemicals are considered as river basin-specific pollutants (RBSP) across the European basins [2, 7]. Such evaluations consist of a comparison of the measured concentration to a critical concentration (the Environmental Quality Standard, EQS), whereby a per-chemical concentration ratio > 1 is interpreted as water quality problem. The per-chemical assessment is combined with an approach known as the "one out, all out" principle for water quality classification, which implies that a water body fails to reach good chemical or ecological status (for PS and RBSP, respectively) if a single chemical has a concentration higher than its EQS [6, 10, 11]. This principle to characterize chemical pollution is used globally since the second half of the twentieth century and has contributed to prioritize measures to improve the surface water quality for the compounds that were identified as water quality threat with this method. However, contemporary chemical monitoring demonstrates the simultaneous presence of hundreds of potentially hazardous anthropogenic chemicals in the water systems of Europe [12], very few of which are PS or RBSP. The risk assessment of these chemicals, required by the WFD due to potential impacts on human health or aquatic ecosystems and their functions, is hampered by the lack of environmental quality standards.

The science of mixture (eco)toxicology is clear: the chemical cocktails encountered in surface waters cause bigger impacts to the environment and human health than each of its components [13]. These observations imply that the use of individual environmental quality standards (EQS) for selected compounds is insufficient to comprehensively judge protection against chemical pollution and that only a holistic, "mixture aware" assessment provides a sufficiently realistic foundation for water quality protection, monitoring, assessment and management [14]. Consequently, the current situation calls for improved mixture risk assessment methodologies, able to make use of the information collected in contemporary chemical monitoring efforts, to identify the likelihood of ecological impacts, identify drivers of mixture risk, and eventually optimize management. In summary, the challenges are to build forth on the strengths of the current system, but also to improve and expand it with regard to (a) comprehensiveness (more compounds) and (b) mixture risk assessment (given the monitoring findings). For practical use, the further challenge is to (c) fit the improved methods to the regulatory context (in Europe: the WFD) and (d) to the practical needs of water quality assessment and management professionals. In the present paper, we describe the expansion of the number of chemicals that can be judged by CBMs. We further provide suggestions on how improved CBMs can be productively used for water quality protection, monitoring, assessment and management, alone or in combination with other lines of evidence, such as outcomes of effect-based methods (EBMs,). We illustrate that outcomes of CBMbased assessments can be summarized and communicated in various ways. First, CBMs can be applied to characterize mixture risks for selected biological quality elements (species groups considered in the WFD), because these end points are considered separately in the assessment of ecological status [6, 14], or individual species (including human health). Second, mixture risks can be characterized as mixture toxic pressure for a species assemblage [15], which relates closely to the protection end point of hazard to the aquatic ecosystem utilized in chemical policies. Finally, CBMs can be used to quantify the chemical footprint of the mixtures emitted to and present in an area [16], to summarize whether the water volume of that area is sufficient to dilute the chemicals that are present to a level that poses negligible harm to the aquatic ecosystem. The use of chemical footprinting is in line with the holistic principles of the WFD, which considers water system level threats and solutions, and provides a way to communicate complex results on mixture risks in easy-to-understand trends (e.g. implementation of a programme of measures causes a trend of reducing the chemical footprint of an area). The type of CBM output that is chosen for an assessment depends on the specific question at hand.

RECOMMENDATIONS

- Implement improved component-based methods (CBMs)—presented below—to assess the likelihood of impacts from pollution with complex chemical mixtures.

- Include all chemicals detected in chemical monitoring programmes [12] and/or predicted by integrated production–emission–fate modelling [17] when assessing mixture risks, and not only those substance for which individual EQS values have already been defined.
- Make an informed choice between established CBM approaches to get insights into the likelihood and magnitude of mixture impacts. CBM approaches described in the literature include (1) mation of risk quotients (RQs), (3) mixture toxic pressure assessments based on species sensitivity distributions (multi-substance potentially affected fraction of species, msPAF), (4) the comparative use of concentration addition and independent action and (5) pharmacologically based mixture models. The choice among these methods should be driven by the intended outcome of the study, as well as the available data and the resources available for generating missing data.
- Utilize the wealth of the world's ecotoxicity data resources. Bridge gaps in the ecotoxicity data with QSAR and read across data. Initiate programmes to close data gaps, especially for chemicals with high potential exposure (high production and emission volumes, combined with physico-chemical properties that might result in increased concentrations in European water bodies) and high hazard (exceeding baseline toxicity).
- Align the use of the CBM methods with the protection and impact end points considered under the WFD in the form of the biological quality elements (BQEs: phytoplankton, macrophytes, phytobenthos, benthic invertebrate fauna and fish).
- Combine the information obtained from CBM with information from effect-based methods (EBMs), ecological studies and in situ tests to identify water bodies at risk of not reaching good ecological status, to quantify impact levels and to identify drivers of the mixture risks [18, 19]. Further investigation should be implemented if a substantial fraction of the impacts observed in the real world cannot be explained by this approach.

- Use CBM based evaluations to explore abatement strategies and/or the expected impacts of future developments in society. Use chemical footprints (derived from CBM results) to summarize and communicate spatial or temporal trends in chemical pollution levels.
- Ensure that results from chemical monitoring efforts as well as the (eco)toxicological information that is needed for applying CBMs are stored in publicly available European data repositories in a format directly useful for applying CBMs. These data collections need to be quality assured, traceable and transparent. They also need to be set up and maintained with a long-term perspective in mind.
- Develop specific regulatory guidance on CBMs for mixture toxicity assessment, to support their consensual EU-wide use in addressing the WFD goals of protecting water quality and reducing the impacts of chemical pollution.
- Apply the improved CBMs in the context of a water system level assessment, given the holistic basis of the WFD.

Several CBMs are available for mixture assessment, sharing common roots but having different data demands and allowing different conclusions to be drawn. It is therefore crucial to make an informed choice among the different CBMs, in view of the available data and resources as well as the specific study question. Reasons for choosing one of the available CBM methods need be worked out and illustrated in specific guidance.

As the implementation of mixture risk assessments in contemporary policies is frequently called for [20] and therefore subject of studies for multiple policy contexts [21], the above recommendations require an appropriate transfer of mixture approaches into the WFD context. That is, assessors should consider that the approaches to mixture assessment and outcome interpretations differ slightly between assessments of effects to species, subgroups of species (such as the biological quality elements of the WFD) and whole species assemblages. It is recommended to take these differences into account, as they may result in interpretation biases, whilst they also relate to communicating mixture risks.

SPECIES-LEVEL ASSESSMENTS

CBMs applied at the level of species are typically based on the classic concept of concentration addition (CA) [22]. CA is also the recommended approach for estimating EQS values for chemical mixtures within the context of the WFD [11]. According to CA, the toxicity of a mixture for a species can be described as the sum of the so-called toxic units (TUs) of all mixture components. Such TUs are simply the ratio of the concentration of a chemical and a defined common (eco) toxicological parameter such as the species' EC50. The validity of summing up TUs for estimating mixture impacts has been repeatedly demonstrated empirically, in an environmental as well as a human health context and for a broad range of bioassays, (eco)toxicological end points and chemicals alike [22, 23]. Although CA is based on the assumption that all components of a mixture share the same mode or mechanism of action, it has been repeatedly shown that the concept also provides useful, but slightly conservative estimates for the effects of mixtures of non-similarly acting chemicals [13]. This is due to the mathematical relationship between the predictions generated by CA and its conceptual counterpart, independent action (IA) [24]. As a result, CA has been suggested as a generic first tier in mixture risk assessment by various organizations (e.g. [22, 25]). If sufficient mode-of-action information and data are available, the comparative application of CA and IA can be used to improve the quantification of mixture risks and to improve the identification of mixture risk drivers [26].

TU sums extrapolate from single-substance toxicities to the toxicity of a mixture. They do not, however, extrapolate between bioassays, (eco)toxicological end points and species. However, in a risk assessment context, data from different closely related species are sometimes mixed. If different effect levels are used for different mixture components, say EC50 and NOEC values, a systematic effect-level extrapolation needs to be incorporated into the assessment. CA-based mixture assessment using TU sums yield a risk estimate for one particular (group of) species only. To estimate ecosystem-wide acceptable exposure levels, CA therefore needs to be applied for each relevant species group. The TU sum for the most sensitive group of species, together with an appropriate assessment factor, can then be used to calculate an ecosystem-wide protective level of exposure. The REACH regulation [9] and the methods used to evaluate water quality under the WFD [11] both revolve around the risk quotient (RQ), i.e. the ratio between an expected or measured environmental concentration and the maximum concentration still considered safe for the whole ecosystem in a given scenario. The latter is termed PNEC (predicted no effect concentration) under REACH and EQS (environmental quality standard) under the WFD. The PNEC considers only ecotoxicological impacts, while the EQS also acknowledges impacts on human health, via the consumption of drinking water and fish. PNECs and EQS values are based on a suite of (eco)toxicological data. After deriving a threshold concentration for these end points, the EQS value for a compound under the WFD is based on the most sensitive end point (i.e. having lowest threshold concentration). This value is then divided by an assessment factor (AF) to cover a range of uncertainties. The final step is then to derive the RQ value, using the (predicted or measured) exposure concentration and the EQS. An RQ < 1 indicates a policy-acceptable level of chemical pollution, while an RQ > 1 indicates reason for concern. The latter situation then triggers follow-up measures, either additional testing or the implementation of risk management measures.

SPECIES GROUPS AND BIOLOGICAL QUALITY ELEMENTS

The WFD considers various species groups to characterize the ecological status of water bodies (biological quality elements, BQE: phytoplankton, macrophytes, phytobenthos, benthic invertebrate fauna and fish). Those species groups are called biological quality elements (BQE). RQ sums have been suggested for mixture risk assessment for species assemblages, which applies to the BQEs, in analogy to using TU sums. However, RQ sums have different characteristics, because the underlying EQS or PNEC values for the compounds in a mixture might be based on different species and/or end point (e.g. the EQS for compound A is based on fish as the most sensitive end point, and for compound B based on invertebrates). The final RQ sum might therefore be a result from summing up different kinds of toxicity estimates for different species. Additionally, the EQS or PNECs of the mixture components are often derived using different assessment factors (the summed RQs of compounds A and B can be calculated, but have no ecological interpretation due to a ‘summing apples and oranges’ effect). Depending on the actual data situation, RQ sums are therefore more difficult to interpret quantitatively [14, 27], except for the fact that they are always equal to or higher than the corresponding TU sums. This still allows using RQ sums as a simple first step to screen for potential ecosystem-wide risks, using only existing PNEC or EQS values. That is: no further action is required if the sum of RQs is below 1. If this is the case, there might be scientific difficulties to explain the meaning of the RQ-value, but there is no doubt about that the mixture exposure requires no further regulatory action. Otherwise, more detailed CA-based assessments should be implemented.

MIXTURE ASSESSMENT FOR THE SPECIES ASSEMBLAGE LEVEL

The RQ methods are applied with the implicit assumption that the concentration–effect curves are straight, and that the sum-RQ represent a quantitative indicator of the magnitude of the mixture risk. However, the concentration– effect curves are not straight, and the sum-RQ can in practice yield very high values, whilst the fraction of species that can be affected is maximally 1. For these reasons, the concept of applying species sensitivity distributions (SSD) and mixture models to derive (mixture) toxic pressures for species assemblages has been proposed [28, 29]. Toxic pressures of chemicals and their mixtures are expressed as potentially affected fraction of species (PAF) or multi-substance PAF (msPAF), with values ranging between 0 and 1. These values are directly relevant for the assessment of impacts, as defined in the WFD-Annex II, where the assessor should evaluate the likelihood (a quantitative concept) of impacts of chemical pollution. Note that the SSD model is also applied to derive environmental quality standards from ecotoxicity test data [11], providing a link between protective assessment goals (and their EQSs) and mixture risk assessment.

SUMMARIZING AND COMMUNICATING MIXTURE RISKS

It is challenging to summarize and communicate the risk information collected for the current set of chemicals considered (a few hundreds), and for the set of monitoring sites with a management area. The assessments yield vast numbers of data points (# chemicals multiplied by # of sampling sites). Methods have been designed to summarize mixture toxic pressure data in the format of the chemical footprint of mixtures in an area [16]. The chemical footprint primarily communicates whether the amount of water in an area is sufficient to dilute the chemicals emitted to that area to a level at which hazards are negligible. By combining this principle with hydrological knowledge, it is possible to not only quantify the size of the chemical footprint for an area, but also to disentangle the relative contributions of upstream and local emissions to the footprint of a water body, and to characterize the net downstream 'export' of mixture toxicity [17].

REQUIREMENTS

All CBMs use (eco)toxicity and exposure information on the mixture components to assess the risks of chemical mixtures. CBMs are therefore applied after establishing the presence of chemical pollution with chemical screening methods [12], or after prospectively evaluating expected pollution trends [17, 30] and possible exposure scenarios that result from the implementation of different abatement strategies [17, 31].
CBM-based mixture risk assessments are only as accurate as the underlying information on the individual substances. Reliable, publicly available information on the (eco)toxicity of the chemicals potentially occurring in the European environment is therefore crucial. This includes commercially relevant chemicals as well as well as non-intentionally produced substances such as combustion products and transformation products. Although regulatory repositories, such as the collection of REACH dossiers at ECHA (*https://echa.europa.eu/information-on-chemicals*, visited May 20, 2019), provide important information, various data collections lack traceability, their contents can change without that being tracked and/or include only a subset of the relevant chemicals. Additional efforts are therefore required to establish a long-term EU-wide repository of (eco)toxicological information for potentially relevant chemicals.
Exposure information is equally crucial for reliable CBM-based mixture risk estimates, which is discussed in detail in accompanying policy briefs [12, 17, 32]. Compiling and documenting the data from existing and future chemical monitoring efforts in a European repository would allow to identify pollution trends as well as the typical mixtures to which particular environments or humans are exposed. The IPCHEM data portal that was recently established by the EU Commission's Joint Research Centre *(https://ipchem.jrc.ec.europa.eu/RDSIdiscovery/ipchem/index.html)* might well develop into such an urgently needed repository on chemical pollution of the European environment.
Pragmatic decisions for data bridging are often needed when applying CBM-based methods, given that consistent data sets are almost never available in a risk assessment context. Given the complexity of the resulting assessments and the number of possible choices for data handling and selecting the various assessment approaches, a thorough and transparent documentation of all input data and the data handling pipeline is crucial. Also, a critical reflection of the overall assessment uncertainty and its explanatory power is needed for each study. Furthermore, integrating the improved and more comprehensive and mixture impact-oriented CBM assessments into both diagnosis (WFD Annex II) and/or surveillance, operational and investigative monitoring for water quality management requires:

- Recognition that water quality problems caused by the societal use of chemicals in principle encompasses the whole 'universe of chemicals' which can be emitted in a significant quantity to a water body, and are thus of societal and regulatory concern.
- Acceptance that novel approaches are essential for problem-defined and solution-focused approaches to handling the chemical pollution problem, which is to be addressed as a mixture problem.
- Recognition that CBMs can be used for evaluation of both the WFD protection (EQS) and impact assessment needs (ecological status) by utilizing quantitative CBM outputs, which can consist of correctly derived and interpreted risk quotients and/or mixture toxic pressures.
- Recognition that the ecotoxicity data that are needed for a comprehensive mixture risk assessment with CBMs require an extension of the data set that are currently adopted for deriving the EQSs for the regulated compounds.
- Guidance on the use of the CBMs for different purposes and the different formats (for species, for biological quality elements, for whole species assemblages) and on the derivation of management plans on the basis of a correct interpretation of CBM-based results.

ACHIEVEMENTS

The SOLUTIONS project has developed and tested the scientific basis for these recommendations, and provides tools and services to utilize them [33].

COLLATION AND CURATION OF ECOTOXICITY DATA TO APPLY CBM

The application of CBMs requires predicted or measured concentrations of chemicals and ecotoxicity data. Exposure data can be obtained from monitoring (e.g. according to WFD-prescribed approaches) or from modelling (e.g. [17]). We produced a curated set of ecotoxicity data (ecotoxicity test data and read-across data) to enable application of CBMs for a wide array of chemicals [15]. The database contains more than 250,000 raw data records—covering a suite of tested compounds and tested species—which can be used for the mixture assessment purposes described below. In daily practice, water quality assessors commonly use 'digested' data, derived from such raw data records. At present, it is not feasible to publish this database, due to the fact that it contains a subset of REACH study results that are in part proprietary (see *https://iuclid6.echa.europa.eu/reach-study-results*, accessed August 13, 2019). The combined data could, however, be used for research when, e.g. median effect data are used. Such uses are described below. Note that the European Chemicals Agency and data owners continue to improve accessibility of the REACH study results, which would change the availability of the raw data set.

UTILIZING THE DATA FOR MIXTURE ASSESSMENTS

The curated data set [15] can be used to derive per-chemical risk quotients (RQ), and thereupon to derive indications regarding the WFD objective of protection against chemical pollution effects.[1] As discussed above, RQ results that are simply based on the ratio of the concentration and the EQS may have no meaningful ecological interpretation towards the type and magnitude of risk of the exposure if $\Sigma RQ > 1$. To address the complexities of interpreting RQ and ΣRQ to evaluate the WFD goals of protection and ecological impact magnitudes, we developed and applied innovative methods, by stepwise removal of causes of interpretation bias [34]. According to this tiered system, the assessor starts with available exposure and effect threshold data (either EQSs, or NORMAN-based PNECs), to evaluate whether $\Sigma RQ < 1$. If so, the assessment can stop, because the mixture risk for the measured compounds implies sufficient protection. If the lowest-tier results in $\Sigma RQ > 1$, the assessor obtains improved mixture risk information by (stepwise) removing unjustified assumptions. Details are explained in [34]. Applied to a series of sites, the approach allows for ranking the expected magnitude of impacts of the mixtures at the sites, so as to help prioritizing measures. Various case studies (see below) were executed with these improved CBM approaches. Note that a Europewide study on chemical pollution was made by Malaj et al. [4], whereby these authors derived the exposure-toeffect quotients for ambient concentrations in European waters to the effect end points of three selected species (LC50 or EC50s for an algal, an invertebrate and a fish species). The results of this assessment showed that ambient (measured) concentrations exceeded the impact end points of those species to different degrees. This provides evidence for the conclusion that organic chemicals likely affect those species if they would be exposed to those water bodies, for individual chemicals. In comparison to an EQS-based assessment in which the RQ is directly derived from the exposure/EQS ratio, this interpretation is straightforward, and not potentially biased by the interpretation problems of the EQS-based mixture assessment methods [34].

ASSESSMENT OF TOXIC PRESSURES OF CHEMICALS AND THEIR MIXTURES FOR SPECIES ASSEMBLAGES

To predict the fraction of species affected by mixtures, SOLUTIONS made expansions and improvements regarding the use of species sensitivity distributions (SSDs) in impact assessment, closely aligned with the WFD-Annex II obligation to assess "the likelihood of impacts". The collated ecotoxicity database (see above) allowed for deriving SSDs for more than 12,000 compounds. The use of SSDs as the CBM method results in the derivation of toxic pressures (per chemical) or mixture toxic pressures (for mixtures), expressed as (multisubstance) potentially affected fraction of species [29]. The research team utilized an expert user modelling pipeline to apply the SSD-based CBM, as described in a project deliverable [35]. An associated (Dutch) project constructed a software tool for Dutch water boards (accessible via *https://www.stowa.nl/publicaties/ecologische-sleutelfactor-toxiciteit-hoofdrapport-deelrapporten-en-rekentools*, "Tool Chemiespoor"; in Dutch). This CBM approach was used in case studies, for example to derive insights into the spatial variation of the (multi-substance) potentially affected fraction

[1] Note that the NORMAN network simultaneously collated and curated ecotoxicity data from various resources, to derive provisional predicted no effect concentrations (PNECs) that can serve the WFD environmental protection goal *(https ://www.norma n-netwo rk.com/nds/ecoto x/)*. NORMAN derived 'lowest PNEC' values for the freshwater compartment for about 40,000 compounds (with a 'verified status' as determined via voting by NORMAN experts for over 1000 compounds; website visited: April 29, 2019). The 'lowest PNEC', similar to the EQS of the WFD, is derived for the water matrix based on data for various end points (human health, secondary poisoning and direct impacts), and converted to 'lowest PNEC' based on expert judgement and data quality-driven application factors.

of species (msPAF) resulting from modelled mixture exposure concentrations across European surface waters [15] and from measured concentration in Dutch surface waters [36]. In the European case study, the model was used to characterize whether mixture exposures are likely to cause insufficient protection, which is based on re-use of the so-called '95 %-protection criterion' (defined as PAFNOEC < 0.05) for mixtures (as msPAF-NOEC < 0.05). The model was also used to provide a quantitative metric that is empirically associated with species loss (msPAFEC50). The derivation of the toxic pressure of chemical pollution utilizes the model used for deriving EQSs in its inverse form [9, 11], implying conceptual consistency between deriving EQSs and toxic pressures. The mixture toxic pressure metric PAF-NOEC relates to the WFD environmental objective of protection, whilst the msPAFEC50 metric empirically relates to impacts on the ecological status [37]. Mixtures matter for ecological status. According to these findings, assessors can use (measured or predicted) concentrations of chemicals in a mixture in combination with the pertinent SSDs and mixture models [15] to derive mixture toxic pressures. Applied to a series of sites allows for ranking the expected magnitude of impacts of the mixtures at the sites, so as to help prioritizing measures.

CASE STUDIES: PRIORITIZATION OF MIXTURE-IMPACTED SITES AND OF CHEMICALS IN MIXTURES

The case study results provide evidence for the applicability of the improved CBMs and the utility of their outcomes for prevention, ranking of mixture impacts across sites and identification of drivers of mixture risks (including currently not considered chemicals) and management.

EUROPEAN AND NATIONAL SCALE

Applied to predicted environmental concentrations for more than 22,000 water bodies situated across Europe, these studies suggested that a large fraction of European surface waters are insufficiently protected against adverse effects of chemical emissions, and that the expected impact magnitude of contemporary pollution (expressed as msPAF-NOEC and msPAF-EC50) varies widely across water bodies [35, 38]. These across-site risk ranking results are in line with the aforementioned assessments of Malaj et al. [4] and results of Kortenkamp et al. [14]. These CBM-based results show that chemical pollution is a stress factor that threatens water quality across Europe, with different expected impact magnitudes across water bodies, and suggesting an important role of mixtures of components that are currently not considered. Moreover, the results presented not only a clear ranking of sites regarding mixture risks, but also the relative dominance of some chemicals in causing that (see also the subsequent example). The derivation of mixture toxic pressures (and the ranking of sites and compounds) is a straightforward assessment which is geared towards large-scale data analyses for water system level analyses. It has therefore not only been applied to predicted exposures, but also to (Dutch) national monitoring data. This yielded national water quality assessment outcomes for mixtures (site and compound ranking), despite differences in sets of monitored chemicals between different water boards [36].

BASIN AND WATER BODY SCALE

Various studies considered mixture risks for water bodies and basins based on measured concentrations. Munz et al. [39] identified CBM-based mixture toxicity differences between sites up- and downstream of wastewater treatment plants, and were able to identify drivers of mixture toxicity. Gustavsson et al. [40, 41] also showed a relative dominance, now for pesticides in Swedish streams and of monitored substances in coastal waters. These authors communicated those results via so-called 'waterfall graphs', to communicate that some chemical are 'drivers of impacts' (Fig. 1). Massei et al. [42] identified mixture risks and drivers for mixtures of pesticides and biocides measured in surface waters of seven large European river mouths. Lindim et al. [43] studied pharmaceutical mixtures in Swedish freshwaters, and also identified key drivers of mixture toxicity. Finally, based on reviews of typically emitted compounds from different land uses, Posthuma et al. [44] simulated the mixture risks of those, providing evidence for different land uses being drivers of mixture 'signatures', again with some compounds dominating mixture risks. That is, different land uses cause vastly different packages of emitted chemicals, and vastly different temporal emission and exposure patterns.

CASE STUDY IMPLICATIONS

All these case studies show that the systematic application of CBM approaches vastly improves the current practice of evaluating chemical pollution in the context of the WFD, in which a limited number of pre-defined priority compounds are assessed one by one. In fact, all the SOLUTIONS case studies flagged chemicals that are not on the WFD list of priority substances or on the corresponding lists of river basin-specific pollutants as mixture risk drivers in various European aquatic ecosystems. Extension of the consideration of a wider array of chemicals is warranted, as all chemicals may threaten the ecological status because all have the potential to cause that (given the observations collated in the ecotoxicity database). It was further shown that mixture risks were often driven by only a few compounds, with the dominant compounds showing strong spatiotemporal variations. Although this, at first sight, could mean that water quality management could focus on a new fixed list of prioritized compounds—those identified as dominant via the CBM analyses—this is not the logical conclusion to be drawn. Every assessment scale (a defined

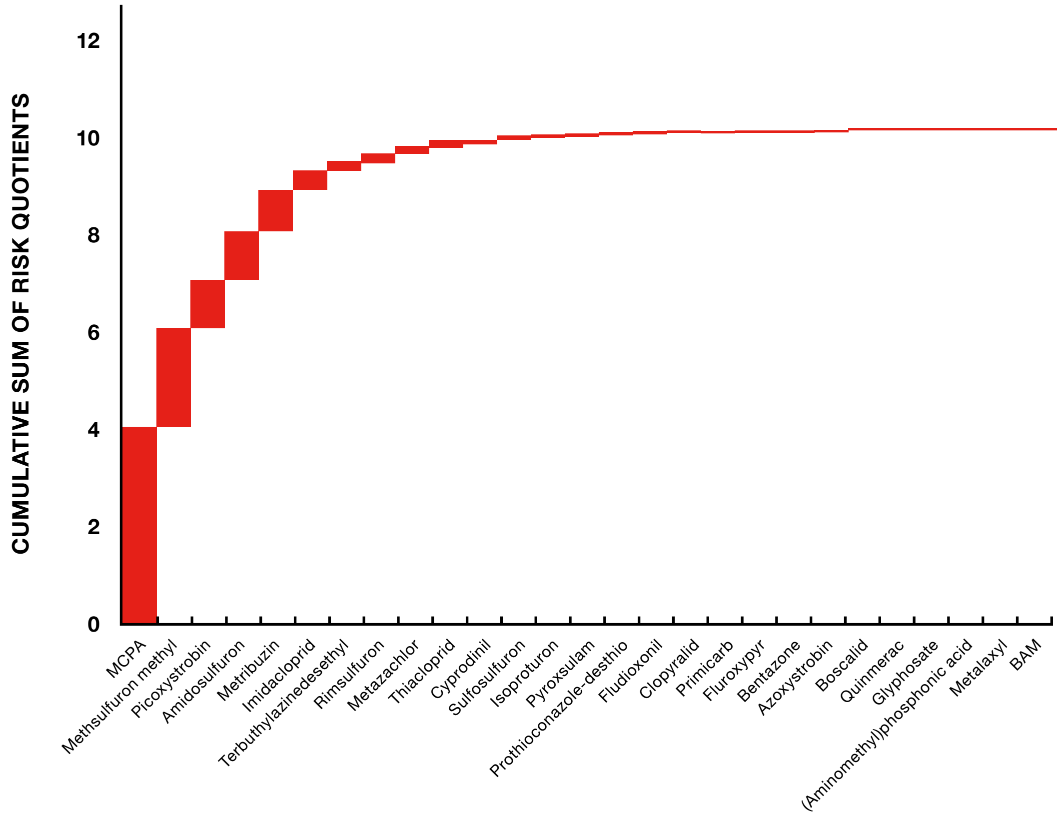

Fig. 1: Example of a 'waterfall graph' (derived from RQ-based analyses derived from the ratio of ambient concentrations of pesticides and the water quality objective) to illustrate the contribution of individual pesticides to the overall mixture risk (adapted from [40])

area, with its emissions and hydrological characteristics) will result in its own rank order of sites and chemicals. We are already used to the fact that different scales result in different priority lists, when going from the European scale (the current 45 priority substances) to the river basin scale (currently approximately 300 river basin-specific pollutants, summed over the EU basins). A further step in downscaling would similarly result in different lists of dominant chemicals for different areas. This process can be followed down till the local water body scale. There only one specific chemical might dominate (e.g. one pesticide in a field ditch), whilst it may be far from dominant for the larger surrounding area (if the pesticide is not used there). Hence, there is always dominance of some chemicals in ambient mixtures, but the dominating chemicals vary among water bodies and over time. The latter follows from dominance changes due to, e.g. pesticide use. The WFD environmental goal of good ecological status may not be reached due to any chemical. Therefore, the WFD text defines pollution as the chemicals (no restriction) that pose a risk to maintaining or reaching the good status (Article 4, and the associated WFD-Common Implementation Strategy (CIS) Document #3, [45]). It appears that the consideration of potentially all chemicals has been lost in practice since the CIS document. Assessors should consider all chemicals and their mixtures, and can apply the improved CBMs to do so.

Scale-dependent identification of dominant chemicals provides the chance to identify effective management steps per certain scale of activities.

ANTICIPATING THE EFFECTS FOR FUTURE EMISSION SCENARIOS AND MITIGATION MEASURES

CBMs can be used to explore foreseeable water quality changes based on future emission scenarios and to predict or retrospectively evaluate abatement success. The former was shown by Van Gils et al. [38]. Exploratory modelling of alternative chemical management scenarios showed a surprising effectivity of a focus on the most hazardous compounds, as identified in chemical safety assessment policies. The latter was also shown by Gustavsson et al. [40]. CBMs can be utilized, therefore, in the context of the solution-focused risk assessment paradigm, which asks for evaluating alternative management or chemical substitution scenarios. CBMs also fit well into the WFD assessment and management cycle [46], as temporal trends in pollution levels can be evaluated. The application of the approach also demonstrated that the risks and relative importance of various compound groups in relation to land use and waste water treatment plants varied [39]. Application to 'think tank' scenarios on future pollution, and evaluation of alternative abatement scenarios, was productive in that it showed which chemical groups and which focus in selecting abatement strategies would reduce predicted impact magnitudes most [30]. These examples also underline how monitoring data (WFD-Annex V) analysed with the CBMs can help to evaluate water quality status and trends. The solution-focused risk assessment approach implies that assessors explore the 'solution space' to define optional risk reduction scenarios [31]. Assessors depend on using the CBMs to evaluate mixture risks under the selected management options (as effect-based methods cannot be applied to expected concentrations), provided that there is a method to predict future concentrations. At present, such a method is available for the European scale [17], and work is in progress to develop a similar model for the Netherlands. For local cases, assessors may use available hydrological information to predict expected concentrations of alternative solution scenarios.

SUMMARIZING AND COMMUNICATING RESULTS ON COMPLEX MIXTURES

SOLUTIONS developed methods to summarize and communicate complex results. For sites, the relative importance of chemicals was suggested to be communicated as 'waterfall graphs', Fig. 1 [40, 41]. For the water system level analyses of chemical pollution, SOLUTIONS developed chemical footprints [16]. Aligned with the SOLUTIONS integrated Model Train, the footprinting allows summarizing local mixture toxic pressure, its origins (whether or not sources upstream contribute to local mixture stress) and its downstream impacts (evaluating effects elsewhere, caused by water flows). Regarding abatement, such summaries are key to assess whether abatement should focus on upstream sources of pollution, on local chemical emissions or on effects of downstream (sensitive) protection end points, or on combinations of these approaches. Currently available results have so far been used to illustrate how this approach operates and what type of results can be obtained [17]. The available EU-wide model can be used to derive these footprint results for selected areas and water bodies.

LESSONS FOR IMPROVED CHEMICAL ASSESSMENTS

The use of CBMs in the case studies clearly emphasized the need for sufficiently sensitive chemical analytical procedures. Ideally, the level of quantification (LoQ) should be around 1/100th of the EQS, or, more realistically, the LoQ should at least approximate the singlesubstance EQS. SOLUTIONS developed and tested the Kaplan–Meier estimation method to handle compounds with insufficiently high LoQs [47]. Also, the expansion beyond the approximate 300 priority substances and river basin-specific pollutants requires additional hazard data. Repositories on hazard data (such as those of REACH, NORMAN, or the SOLUTIONS curated database of effect data) can be used as a source of such data for the CBM applications, provided that various key aspects are considered. Those are—at minimum—that ecotoxicity data used for a CBM could represent outdoor exposure conditions, and that data used have a transparent and reproducible origin [15, 47]. The consequences of neglecting proper management and choice of (eco) toxicity data are large, as presented in the report of Arle et al. [7]. These authors reported an array of EQS values for RBSP across European basins, whereby the minimum and maximum EQS values for one-third of the listed substances differed up to 10-fold from each other across countries, and more than half (53 %) of all the substances differ by more than 10-fold and up to 105- fold from each other. This relates in part to the use of different assessment factors for deriving EQSs.

In general, the practical experiences from the case studies clearly emphasize that the ecotoxicity data repositories that form the basis for all CBM-based methods require substantial improvements in transparency, traceability, consistency and, last but not least, data quality.

THE NEED FOR THE USE OF IMPROVED CBMS

The current use of CBMs has two impacts on water quality assessment practices that negatively affect the likelihood of reaching the WFD environmental goals. This is caused by the fact that the indicator system sensitively reacts to extra chemicals becoming monitored and is at the same time highly insensitive to water quality improvements that occur upon abatement investments. These act as 'hidden triggers' that counteract reaching the WFD environmental objectives, as the first makes the assessor reluctant to add compounds to a monitoring plan and the second makes the assessor reluctant to invest in abatement as improvements remain hidden. The use of only two classes for chemicals (an exposure concentration is classified as either lower or higher than the EQS) is the root cause of this practical problem. The proposed improved CBM methods [14, 15, 34] provide refined insights into chemical pollution, required to inform managers on the needs to take protective or restorative management action. The quantitative insights provided by the improved CBMs deliver key insights for management prioritization and planning. The SOLUTIONS case studies showed this and how the use of the improved CBMs substantially— and the resulting ranking of mixture risks among sites and compounds— refines the information for water management prioritization and planning. Examples of the improved efficacy of refined CBM approaches outside SOLUTIONS have started with a landscapelevel 'one pesticide' assessment for water bodies across the USA in 1996 [48]. Today, such assessments have expanded to mixtures and they are currently in the stage of gaining global appreciation (examples listed in [15]).

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at https://doi.org/10.1186/s12302-019-0246-5.

Abbreviations

AF: application factor; AS: assessment factor; BQE: biological quality elements; CA: concentration addition; CBM: component-based method; EBM: effectbased method; EC50: effect concentration related to an effect of 50 % on a selected end point; ECHA: European Chemicals Agency; EQS: environmental quality standards; LoQ: Level of quantification; msPAF: multi-substance potentially affected fraction of species; NOEC: no observed effect concentration; PNEC: predicted no effect concentration; PS: priority substances; QSAR: quantitative structure activity relationships; RBSP: river basin-specific pollutants; REACH: Registration, Evaluation, and Authorization of Chemicals; RQ: risk quotient; SPR: Strategic Program RIVM; SSD: species sensitivity distributions; TU: toxic unit; WFD: Water Framework Directive.

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POLICY BRIEF

solutions

INCREASE COHERENCE, COOPERATION AND CROSS-COMPLIANCE OF REGULATIONS ON CHEMICALS AND WATER QUALITY

ABSTRACT

An analysis of existing regulatory frameworks for chemicals reveals a fragmented situation with a number of regulatory frameworks designed for specific groups of chemicals; for protection of different end-points and covering different parts of the chemicals´ life cycle stages. Lack of- and fragmented information on chemicals (properties, use, emissions as well as fate, occurrence and effects in the environment) limit the ability for assessment and early action, and existing legislation would benefit from more transparency and openness of information and knowledge. More holistic and efficient development and implementation of existing legislation can be achieved by better cooperation, harmonisation and information exchange between different regulatory frameworks and by improved science–policy interactions. The introduction of an organisational structure and incentives for cooperation are proposed. Cooperation should focus on harmonisation of advanced monitoring activities, modelling, prioritisation, risk assessment and assessment of risk prevention ('safe by design') and minimisation options. A process for dialogue and information exchange between existing policy frameworks and with stakeholders (industry, NGO´s, etc.) should be included to identify feasible options for mitigation as well as regulatory gaps—on local and EU-scales. There is also a need to increase international cooperation and strengthen global agreements to cover the full life cycle of chemicals (produced and consumed globally) and for exchanging knowledge and experiences to allow early action. This recommended action would also provide knowledge and a framework for a shift towards a sustainable chemistry approach for chemical safety based on a "safe by design" concept.

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CHALLENGE

The focus of this study is the Water Framework Directive (WFD) and how to implement and develop legislation to ensure the protection of European waters from chemical contaminants. Many of the potential chemicals threats to water quality are, however, regulated under other regulatory frameworks, or not at all, and the starting point is thus an overview and assessment of existing legislation on chemicals focussing on other areas than water quality. Several regulatory frameworks (EU Directives and Regulations, international agreements and Conventions), which aim to prevent and reduce risks and impacts of chemicals and their mixtures to both the environment and human health, have been developed and implemented over the last decades [1]. These regulatory frameworks have different and sometimes overlapping scopes covering chemicals (as such or in mixtures) in articles, emissions or concentration levels in the environment on different geographical scales (local, regional and global). The regulatory frameworks are also developed for specific parts, or the whole, life cycle of the chemicals or for ecosystem protection as depicted in Fig. 1. The number of chemicals regulated per framework spans from only a few to thousands of substances, whilst potential cumulative effects of substances in mixtures are often not or only partially considered or assumed to be covered by application of uncertainty or assessment factors in the risk assessment. In some of the frameworks, the regulated chemicals constitute an important fraction of the total number of chemicals used in society and present in the environment. In other legislation, focus is on a smaller subset of chemicals, which are considered to pose the highest hazards. Different frameworks also focus on different end points, e.g. risks for human health, ecosystem effects or both, and account for different contexts (e.g. plant protection products in relation to food production). Therefore, they apply different procedures for identifying these potential risks to compare with different forms of benefits. The mixture risks are often neglected (although possibly covered indirectly by the application of uncertainty or assessment factors in risk assessment) despite the common co-occurrence of many chemicals in the environment, the goal of the non-toxic environment [2] and EC-incentives to consider mixtures [3].
Chemicals that are not regulated in terms of desired environmental quality but represent a potential risk are sometimes denoted as emerging chemicals or Chemicals of Emerging Concern (CECs). CECs present in the environment are not necessarily new chemicals. They can also be substances that have been present in society and the environment for a long time but whose presence and potential impacts are now being elucidated. The continued appearance of emerging chemicals from new or newly detected sources and with varying properties will require continuous adaptation and updation of current regulatory frameworks, complemented with a pro-active ‘safe by design’ and ‘sustainable chemistry’ approach. It will also require continuous adaptation of risk assessment and management to ensure protection of human health and the environment.
The Water Framework Directive (WFD) has a strong focus on status assessment, with a chemical status defined on the basis of a small set of priority substances (PS), among them many legacy and ubiquitous chemicals with frequent Environmental Quality Standard (EQS) exceedance. These are chemicals for which no straightforward management options exist. According to the “one-out-all-out” principle this means that the chemical status cannot be improved with existing management although there are plenty of abatement options that would significantly reduce the risk to ecosystems and human health posed by the mixture [4]. Thus, incentives and solution-focused approaches are required to improve water quality even if the final goal of a good chemical status cannot be achieved yet.
Identification of CECs by means of advanced monitoring or modelling approaches requires both expert knowledge and resources. Not all individual countries or water district authorities currently have these capacities, whilst coverage of the increasing number of chemicals in commerce remains a challenge in itself. Increased cooperation and knowledge sharing on methods and procedures for monitoring and modelling as well as for the development of efficient abatement strategies and action plans are necessary.

RECOMMENDATIONS

An innovative and comprehensive regulatory framework for chemicals should be designed and implemented, based on a solution-focused approach and building upon existing legislation. The approach should focus on linking conventional prospective risk assessment of individual compounds with retrospective risk assessment for environmental compartments, but also on evaluating which measures can best be taken to avoid and prevent novel risks or reduce existing risks. This concept for a solution-focused approach was introduced by the U.S. National Academy of Sciences [5] to improve the utility of risk assessments and has been further elaborated in the SOLUTIONS project with the WFD as the starting point [6]. The project has provided methods and tools for implementing such a solutions-focused approach, i.e. for testing and evaluating water quality by both monitoring and modelling and for identifying abatement options.
This approach implies a continual work with focus on operational prevention and reduction of chemical risks applied to any stage of the life cycle of a chemical. It also ensures that adequate measures can be taken when need arises or when feasible to gradually reduce risks for exposures in a stepwise manner.

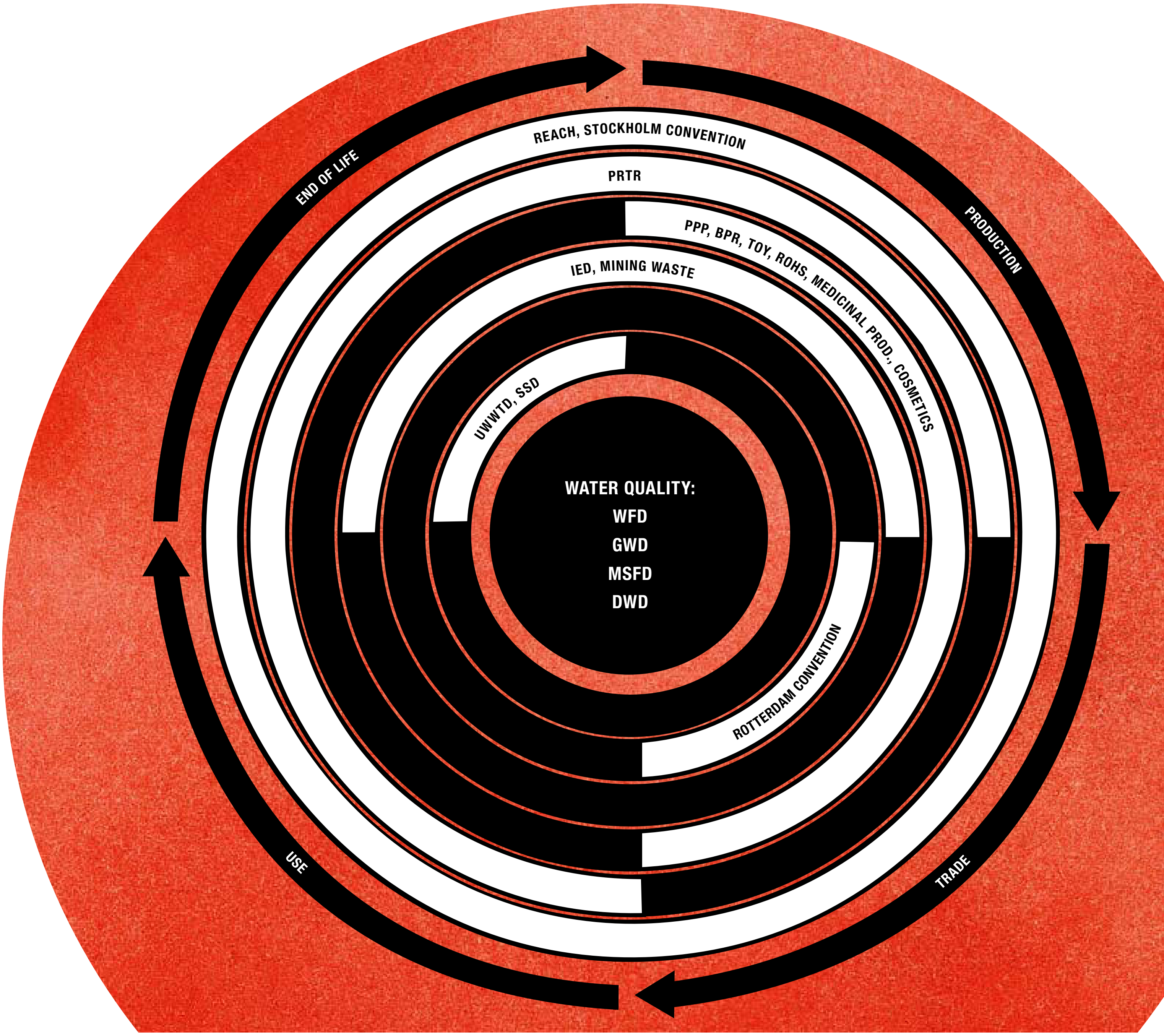

Fig. 1: Graphic representation of the life cycle of chemicals (black) and coverage by different regulatory frameworks (white = covered, black = not covered, see list of abbreviations below). The centre represents four regulatory frameworks addressing chemical pollution and water quality [1]. BPR—Biocidal Products Regulation (EC/528/2012); Cosmetics—Cosmetic Products Regulation (EC/1223/2009); DWD—Drinking Water Directive (98/83/EC); GWD—Ground Water Directive (2006/118/EC); IED—Industrial Emissions Directive (2010/75/EU); Medicinal Products—Regulation on Procedures for the authorisation and supervision of Medicinal Products for human and veterinary use and establishing a European Medicines Agency (EC/726/2004; Mining Waste—Mining Waste Directive (2006/21/EC); MSFD—Marine Strategy Framework Directive (2008/56/EC); PPP—Plant Protection Products Regulation (EC/1107/2009); PRTR—European Pollutant Release and Transfer Register (E-PRTR), *https://prtr.eea.europ a.eu/#/home*; REACH—Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (EC/1907/2006; RoHS—Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment. *https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32011L0065*; Rotterdam Conv—Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade; SAICM—Strategic Approach to International Chemicals Management SSD—Sewage Sludge Directive (86/278/EEC); Stockholm Conv.—The Stockholm Convention on Persistent Organic Pollutants; Toys—The Toy safety Directive, *https://ec.europa.eu/growth/sectors/toys/safety_en*; UWWTD—Urban Waste Water Treatment Directive (91/271/EEC); WFD—Water Framework Directive (2000/60/EC).

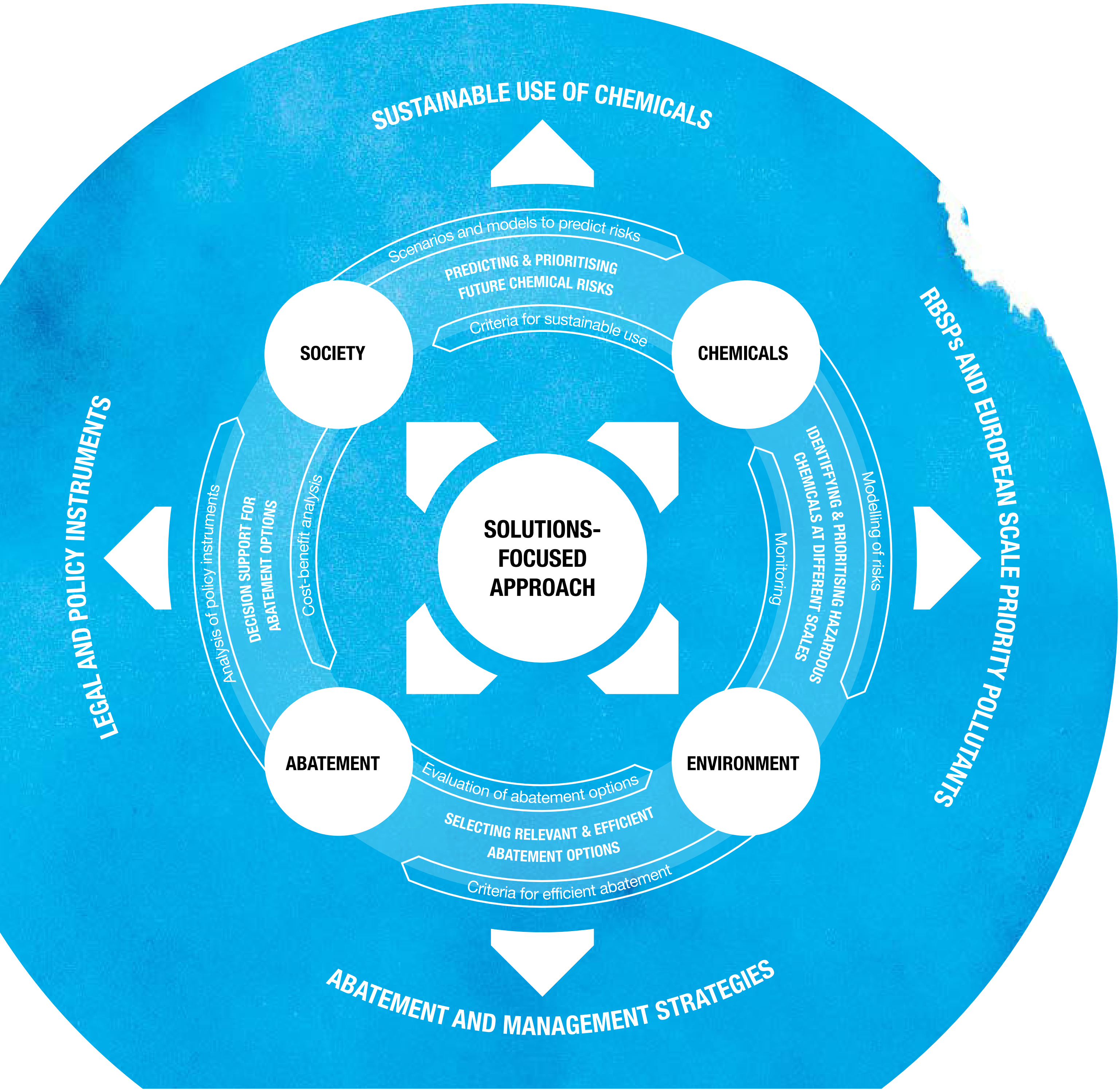

Fig. 2: The conceptual framework for operationalizing the solutions-focused approach, illustrating how it assists in risk assessment and management of chemical pollution in relation to water quality [8]. RBSP River Basin-Specific Pollutants.

The solutionfocused approach and the knowledge gained by applying it, can also provide a basis for a long-term shift towards risk reduction via 'safe by design' approaches [7].
The solution-focused approach also entails a strong link between knowledge on chemical use and occurrence in society, emissions and presence in the environment and associated exposure of nature and humans, as illustrated in the conceptual framework (Fig. 2, upper and lower right). Chemical and environmental risk information is collected and combined to design and evaluate abatement options and developments in society (Fig. 2, lower and upper left). This necessary integration could, to a large extent, be achieved by better linking existing prospective regulatory frameworks (e.g. REACH, PPP, BPR) with those more focused on assessing and protecting the environment (e.g. WFD). Prospective regulatory frameworks generate information on use patterns and amounts and regulate the use of potentially hazardous chemicals via authorisation or restrictions. By combining these legal instruments for reducing releases to the environment and resulting exposures with the application of advanced monitoring for assessing the status of water bodies, a scientifically sound and more comprehensive basis for action can be developed.
To implement a solutions-focused approach as an overarching principle for implementing regulations, several recommendations can be given:

- Introduce a common strategy and an organisational framework for cooperation and action to prevent and reduce risks of emerging substances. This should build on existing legislation and existing structures and should include the following components (related to Fig. 2):

Chemical safety assessment: Develop and apply harmonised procedures for assessment, prioritisation, and identification of CEC utilising experiences and knowledge from both prospective risk assessment and environmental quality assessment.
Environmental quality assessment and management: Initiate and promote cooperative programs and activities for advanced monitoring and modelling based on harmonised methodologies for CEC in European waters and other ecosystem compartments.
Abatement options and efficacy: Develop a common information platform for storage and retrieval of information on abatement options (technical and non-technical measures), enabling exchange of information and experiences between different stakeholders.
Society: Engage in dialogue between stakeholders and different regulatory bodies to identify actions to prevent and reduce the production, use and emissions of hazardous compounds and to identify the needs for policy evaluation and adaptation

- Specifically, for improved implementation of the WFD, current status assessment with should be complemented with incentives and guidance for a solution- focused approach to identify abatement priorities and to reduce risks of chemical mixtures, even if good chemical status cannot be achieved. Consider new policy instruments beyond the exceedance or non-exceedance of EQS for individual compounds that demand for and reward progressive improvement of water quality. With effect-based monitoring [9], chemical screening [10] and models [11] to identify potentially hazardous chemicals, componentbased methods for mixture risk assessment [12] and ecological tools [13] results from the SOLUTIONS project provide the necessary means to detect and quantify the progress.

Engagement of all relevant stakeholders including industry, agriculture, scientific community and public representatives is a necessity for the above approach to be implemented successfully.
In a slightly longer perspective, it will become necessary to introduce a more pro-active approach by promoting and requiring 'safe by design' and 'sustainable chemistry' before introducing new substances on the market. The current approach with mainly per-chemical safety assessment can thus gradually be replaced.

REQUIREMENTS

To support the solutions-focused approach for the WFD, whilst including potentially more than 145,000 chemicals [14] and their mixtures, sharing of information on use, properties occurrence and environmental and human exposure of CEC is necessary, to embody a sensible prioritisation of management action. Mandatory monitoring and modelling covering all EU member states and all water bodies with the aim to identify potentially all CECs is not realistic in the short term due to costs and efforts required. Nevertheless, increased ambitions and efforts by member states on monitoring, modelling and (mixture) risk assessment are required. To support this and to ensure knowledge exchange joint European efforts should be encouraged. An organisational structure and a science–policy interface would be required for harmonising and increasing the efficiency of efforts to prevent and reduce chemical contamination of European waters.
The following activities are proposed as the main components of a joint European program for monitoring, modelling, assessment and abatement of chemical contamination of European Waters:

- Collaborative efforts for advanced monitoring and data sharing: Modern analytical tools, e.g. Effect- Directed Analyses (EDA), Non-Target Screening (NTS), and arrays of bioassays are increasingly applied to identify chemical compounds with potentially adverse effects on the aquatic environment [9, 10]. Applied methods often require

significant resources and knowledge and results may depend on the choice of a specific method for an individual case. This activity provides knowledge-transfer and works for harmonisation of methods, knowledge sharing and science to policy communication to facilitate a maximised use of knowledge and data gained for further risk assessment, prioritisation and assessment of mitigation options.
- Modelling fate and distribution of chemicals across the EU: Modelling is a useful complement to monitor for bridging gaps in geographical and temporal coverage of monitoring and identifying potential risks from CECs not included in monitoring programs [11]. This activity provides data and guidance to identify" no, low, or negligible risk" chemicals, to guide monitoring efforts (selection of substances and sampling sites) and to interpolate between results from monitoring which are limited to specific sites and points in time. In addition, modelling can also be used to simulate the outcome of different abatement scenarios to support the selection of the most effective way forward.

In addition to a modelling and monitoring centre, a coordinated activity on assessment, abatement and legal instruments is also proposed. This activity would have as focus:

- Assessment of the current status and the needs and options for abatement, using concepts and modelling methods for chemical footprints [13], linking chemical and ecological status as well as mixture exposure and effects. The results of these efforts would support the implementation of existing legislation by assessing and evaluating potential abatement options including technical and non-technical measures [15, 16].

ORGANISATIONAL ASPECTS

The application of CBMs requires predicted or measured The proposed actions should build upon the considerable experiences and knowledge gained from existing activities on monitoring, modelling and assessment of chemical status by, e.g. dedicated efforts in member states and by engaging the scientific community.
The work performed under the Common Implementation Strategy (CIS) of the Water Framework Directive (EC 2000) (2000/60/EC) can be taken as a good example of collaboration. The CIS was developed to allow a coherent and harmonious implementation of the Directive with focus on methodological questions on technical and scientific issues. A number of Guidance Documents have been prepared including several on monitoring *(https://ec.europ a.eu/environment/water/water-framework/facts_figures/guidance_docs_en.htm)*. The guidance documents are non-binding and are directed to experts who are directly or indirectly involved in implementing the Directive.

For non-regulated substances, the NORMAN network *(https://www.norman-network.net/)* provides an existing platform for chemical monitoring, prioritisation and risk assessment—including, e.g. development of methods, knowledge sharing and sharing of information on results of monitoring. For monitoring data, the EU has also has launched the Information Platform for Chemical Monitoring (IPCHEM) where data are made available under four modules: Environmental monitoring, Human Bio-Monitoring, Food and Feed, Products and Indoor Air *(https://ipchem.jrc.ec.europa.eu)*. Other examples of international collaborations such as the Joint Danube Survey *(https://www.danubesurvey.org/jds4/)* organised by the International Commission for the Danube River *(https://www.icpdr.org/main/)* and joint monitoring programs organised by the International Commission for protection of the Rhine river *(https://www.iksr.org/en/)* can also serve as good examples of existing cooperation. The European Environment Agency (EEA) should also have a central role in integrating knowledge and identifying needs for action, as detailed in *https://www.eea.europa.eu/highlights/more-action-needed-to-tackle*.
There is currently no organisational structure for joint international modelling activities of CEC but a starting point would be to coordinate existing initiatives in the scientific community. This component can potentially be aligned with and become integrated with the current NORMAN network activities.
The previously proposed activities should be linked to the on-going efforts by the European Commission to evaluate and improve existing legislation *(https://ec.europa.eu/environment/chemicals/indexen.htm)* with increased efforts to establish links between, e.g. the WFD and REACH and other relevant legislation as well as with global agreements such as Stockholm Convention and SAICM. The EU-goal of a non-toxic environment by 2020 [2] requires swift advancements of approaches for safe chemical design, not limited to some few but including all chemicals on the EU market.
A key factor of the solutions-focused approach outlined above is that it can also be introduced and implemented on a local scale. By combining local knowledge on sources of emissions and water quality status, and by engaging local stakeholders in dialogue, rational and realistic solutions to identified problems of chemical contamination of local water bodies can be identified and implemented.

ACHIEVEMENTS

The SOLUTIONS project used the solutions-focused approach based on the Conceptual Framework to achieve significant progress in providing science-based and application-ready methods related to protection, monitoring, modelling and abatement of CEC, whilst also evaluating future societal developments and emerging (mixture) risk to anticipate on measures needed to avoid future damage. The results of the SOLUTIONS project can be found at RiBaTox [17], accessible at https://solutions.marvin.vito.be/, which helps to select and use SOLUTIONS Tools and Services that relate to the diversity of water-related challenges. RiBaTox is a practical example of the translation of the solutions-focused approach into a web-based tool. Recommendations on how to implement these scientific developments for a further development of the WFD have also been formulated [18]. A number of these results also forms the basis for specific recommendations on, e.g. Effect-Based Methods [9], emission, exposure and effect modelling [11] and technical- and non-technical abatement [15].

In addition to the assessment of chemicals' life-cycle coverage by different regulatory frameworks as presented in Fig. 1, existing regulatory frameworks differ since they are developed for specific groups of chemicals and for protection of different end-points. An increased efficiency could be achieved if all regulatory frameworks considered protection of both human health and the environment. Cooperation between existing regulatory frameworks on, e.g. exchange of information on use, emissions, occurrence and effects in the environmental can also give rise to a more coherent and efficient regulation. Another step towards cooperation and harmonisation would be to introduce common procedures for risk assessment and prioritisation. And as the market for chemicals is global, there is a need to discuss chemical management on a global level and thereby strengthen the cooperation between EU and relevant international organisations. Information on the different regulatory frameworks and regulated substances can be found in the form of a database accessible at https://apps.ivl.se/solutions and via www.solutions-project.eu. The need for database support on which substances are regulated has recently been recognised by the European Commission who have announced the development of a website providing information on EU-legislation for different chemicals to be launched in 2020 https://newsletter.echa.europa.eu/home/-/newsletter/entry/which-pieces-of-eu-legislation-apply-to-your-substances.

Building on the Conceptual Framework designed in an early stage of the SOLUTIONS project to define necessary components of the solutions-focused approach to chemical regulation [8], (Fig. 2) the SOLUTIONS project has shown that the necessary knowledge base needed for a more proactive and efficient regulation for risk minimisation from CEC is available and achievable.

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at https://doi.org/10.1186/s12302-019-0235-8.

Abbreviations

BPR: Biocidal Products Regulation (EC/528/2012); CEC: Chemicals of Emerging Concern; Cosmetics: Cosmetic Products Regulation (EC/1223/2009); DWD: Drinking Water Directive (98/83/EC); EDA: Effect-Directed Analysis; EEA: European Environment Agency; EQS: Environment Quality Standards; GWD: Ground Water Directive (2006/118/EC); IED: Industrial Emissions Directive (2010/75/EU); IPCHEM: EU Information Platform for Chemical Monitoring; Medicinal Products: Regulation on Procedures for the authorisation and supervision of Medicinal Products for human and veterinary use and establishing a European Medicines Agency (EC/726/2004); Mining Waste: Mining Waste Directive (2006/21/EC); MSFD: Marine Strategy Framework Directive (2008/56/EC); NORMAN: Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances; NTD: Non-target screening; PPP: Plant Protection Products Regulation (EC/1107/2009); PRTR: European Pollutant Release and Transfer Register (E-PRTR), https://prtr.eea.europa.eu/#/home; PS: Priority substances; REACH: Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (EC/1907/2006); RoHS: Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32011L0065; Rotterdam Conv: Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade; SAICM: Strategic Approach to International Chemicals Management; SSD: Sewage Sludge Directive (86/278/EEC); Stockholm Conv.: The Stockholm Convention on Persistent Organic Pollutants; Toys: The Toy safety Directive, https://ec.europa.eu/growth/sectors/toys/safety_en; UWWTD: Urban Waste Water Treatment Directive (91/271/EEC); WFD: Water Framework Directive (2000/60/EC).

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POLICY BRIEF

solutions

THE RIBATOX WEB TOOL: SELECTING METHODS TO ASSESS AND MANAGE THE DIVERSE PROBLEM OF CHEMICAL POLLUTION IN SURFACE WATERS

ABSTRACT

Chemical pollution of water bodies is a complex problem around the globe. Research has provided a novel assessment paradigm (solution-focused risk assessment) and novel data, measurement methods and models to improve on current practices. Their adoption and application require establishing novel linkages between the diverse problem definitions and the novel approaches. That would assist water quality professionals to select the most effective option or options to protect and restore water quality. The RiBaTox (River Basin Specific Toxicants assessment and management) web tool consists of short descriptions of the novel approaches and a decision tree for end-users to select those. The overview of novel approaches collated in RiBaTox is relevant for end-users ranging from local water quality experts up till strategic policy developers. Although RiBaTox was developed in the context of European water quality problems, the methods provided by RiBaTox are relevant for users from (inter)national to local scales. This paper is part of a series of Policy Briefs from the EU-FP7 project SOLUTIONS *(http://www.solut ions-proje ct.eu)*, which provide backgrounds on chemical pollution of surface waters and policy practices and proposed improvements.

CHALLENGE

Chemical pollution in European water resources is of growing societal concern due to the potential risks to ecosystems and human health [1, 2]. The pollution problem can vary from simple and local, to complex and basin-wide. In 2010, the EU funded a substantial body of research activities to improve on the approaches for diagnosing and managing chemical pollution for surface waters in Europe [3]. In response, the SOLUTIONSproject *(http://www.solut ions-proje ct.eu*) undertook fundamental research in water pollution. Results were evaluated in the context of, and aligned with, the current regulatory framework (the EU-Water Framework Directive [4]). This resulted in (a) a proposal to improve the utility of chemical risk assessments, a (b) suite of improved or novel technical tools and services to diagnose water quality problems with chemicals, and (c) a proposal of a strategy and a solutions database to translate diagnostic results in a programme of measures [5].

The results may lead to changes to current practices. As yet, the methods to assess chemical pollution problems are commonly applied in a straightforward way. That is, monitoring efforts yield data on measured concentrations of chemicals, and the observed values are compared on a per-chemical basis to a protective environmental quality standard. Amongst others, this involves an analysis of pressures and impacts [6] and the classification of the chemical and ecological status on the basis of chemical and ecological monitoring data and the quality standards [7, 8]. The current approach does not sufficiently cover the chemical pollution problem, as both societal concerns and scientific research asks consideration of far more chemicals and their mixtures [9, 10]. The results of the research encompass a suite of tools to characterize the pollution problem, as described in associated Policy Briefs of the SOLUTIONS-project. Due to the diversity of the new opportunities and the need to change the current practice, their practical implementation might be challenging for experts involved in chemical pollution assessment and management. These challenges might be faced by experts who are involved in the day-to-day practices of monitoring, assessment and management at the level of a water board up till decision makers working on the long-term strategic planning to prevent and reduce chemical pollution via, e.g. improved regulations or the provision of applicable guidance documents. Building forth on the current practices, the new opportunities for diagnosis confronts them with the choice to address the chemical pollution problem diagnosis, e.g. with improved component-based methods [11], or effect-based methods [12], or ecological methods [13], or any combination thereof.

Given the project results, the practical challenge boils down to the question of how to support the process of matching the novel assessment approaches to the diverse chemical pollution problems for the diverse end-users.

To address this problem, the SOLUTIONS-project designed the RiBaTox (River Basin Toxicants assessment and management) web tool. Despite the tools' name suggest a limitation to river basin-specific pollutants (a group of chemicals specifically considered within a river basin) in the EU-WFD context, the web tool provides information for any spatial level and for all surface waters globally. The WFD itself has no scale limitation, as any chemical may locally threaten the ecological status; if so, that chemical is identified as 'specific chemical' against which measures much be taken to reduce those impacts (see also [6]).

The RiBaTox web tool was designed to provide a decision tree and fact sheets that describe the novel assessment methods. Despite the EU-context of the SOLUTIONS research, the applicability of the methods is not limited to the EU only. The contents of RiBaTox are applicable to any water management situation, whether local, regional or (inter)national. The decision tree and the methods were derived in the context of the solutionfocused risk assessment paradigm [5, 14]. This paradigm is used to improve the utility of the risk assessments and has been the basis for a strategy and a database that provides end-users with solutions options for water quality management planning. The fact sheets can be updated in response to novel practical needs or results of research. RiBaTox is available via *https://solutions.marvin.vito.be/*.

RECOMMENDATIONS

To assist water quality protection, monitoring, assessment and management in practice, water quality managers and policy makers are recommended to:

- Use the SOLUTIONS conceptual framework for protecting, assessing and managing surface water pollution with complex mixtures, and consider RiBaTox as operational tool to use this conceptual framework in practice;
- Use RiBaTox to navigate from the specifications of a (likely) water pollution problem towards the diagnostic tools and services with which that problem can potentially be assessed and managed, and to identify the best (combination of) tool(s) that serves the purposes best;
- Apply RiBaTox for making decisions on the design of monitoring campaigns, on prioritizing chemicals, sites and abatement options, on the use of models to bridge data gaps and to prioritize them for the need of experimental efforts to fill them;
- Use RiBaTox as a basis for the development of a longstanding and regularly updated information platform that reflects the newest knowledge and further develop the structure of solutions-oriented decision trees with informative fact sheets as end points.

REQUIREMENTS

Any tool or service needs to be useful, known, accessible by stakeholders and actual. The requirement of potential usefulness is that the web tool allows stakeholders to find science-based proposals to address the wide array of chemical pollution problems, beyond the methods currently known and frequently used. The set of tools and services can be used by experts at any level of organization— be it those that are responsible for local water quality management or those working as strategic policy designers at the level of countries or the EU.

The other requirement of 'being known' is reflected in the web tool (and the present paper). Scholars and practical end-users can find and use the available knowledge on approaches to investigate surface water chemical pollution. The requirement of accessibility of the web tool has been arranged until at least 2020 via the SOLUTIONS Web site (*https://www.solutions-project.eu/)*. Longer-term maintenance and regular updates are achieved with the European science-policy network on emerging pollutants NORMAN *(https://www.norman-network.net/)*, which acts as RiBaTox host.

The requirement of actual information is organized via the potential to update to information in RiBaTox. Active management of RiBaTox is recommended to continue that assessors can identify contemporary tools and services for their chemical pollution problem specification. Such management could be based on testing and implementing continuous improvements as needed. Systematic management would advance the system and its utility for water quality assessment and management beyond the duration of the SOLUTIONS-project, aligned with the longer-term requirements of the WFD and/or of other (inter)national water management schemes.

ACHIEVEMENTS

RIBATOX AS VERSATILE AND ACTUAL WEB TOOL

The goal that novel and diverse science-based approaches for chemical pollution assessment and management can be found by end-users has been achieved by creating the RiBaTox web tool.

The web tool concerns a specific policy area, which is chemical pollution of surface waters. The web tool assists end-users in understanding solution-focused risk assessment (with early focus on the 'solution space' when a pollution problem is encountered), in identifying potential diagnostic tools and services to diagnose the relevance of mixtures and individual chemicals in affecting water quality, and in the combination of both in selecting measures to prevent or reduce chemical pollution. The latter are required for the programmes of measures, which are the key management step in the assessment/management cycle for improving water quality.

The web tool supports the recommended changes of chemical pollution protection, assessment and management that have been proposed in associated Policy Briefs (e.g. on using holistic approaches considering chemical pollution from a water-system level point of view [5], for vastly more chemicals and their mixtures [10–12], via both monitored and modelled environmental concentrations of chemicals [15], with early consideration of the 'solution space' [16, 17], and with associated improvements on, e.g. monitoring data management [18]).

The web tool consists of a decision tree (to identify and select available tools and services for diagnosis) and of a set of fact sheets (available also as Additional file 1 to this paper). RiBaTox supports end-users in applying the novel science-based tools and services, fully in line with the obligations of the regulations to protect and restore surface water quality.

For example, if an end-user is confronted with evidence for chemical pollution—e.g. from an analysis of the drivers of chemical emissions in an area—and is specifically interested in impacts, the web tool shows potential approaches to be component-based methods, effect-based methods or ecological tools. All three can be used from a scientific perspective, as all three are a line of evidence on the presence of impacts. All three can also be used from the regulatory perspective of water quality management, as most regulations specifically suggest collecting data on multiple lines of evidence for this (e.g. WFD, Annex II). The assessor can select either individual methods or combinations of methods for the specific conditions of the pollution case. The web tool and the fact sheets can be updated to novel scientific insights or societal/regulatory needs if needed.

ALIGNMENT BETWEEN THE SOLUTION-FOCUSED APPROACH AND RIBATOX

The research achieved to use the solution-focused risk assessment paradigm as basis for the design of RiBatox decision tree and the fact sheets on the diagnostic tools and services. According to the conceptual framework for solution-focused risk assessments [16], the problem of- and solutions for chemical pollution can be explored from different angles (chemicals, environment, abatement and society, see also [5]). The RiBaTox web tool reflects the different angles of the conceptual framework in the decision tree and the presence of fact sheets related to all the framework angles. It provides information on, e.g. monitoring strategies, modelling strategies, prioritization strategies, abatement strategies and policy strategies. Those strategies not only enable to find approaches or models for the various purposes, but also the data sets that have been compiled to serve as a harmonized volume of information for the different uses, available to all.

THE COMPILATION OF CURRENT DIAGNOSTIC TOOLS AND SERVICES IN RIBATOX

More than 80 potentially relevant tools and services were identified in the research. This expands vastly on the current practices, in which classification of chemical and ecological status on the basis of monitoring data is common [2], but where the consideration of multiple lines of evidence and comprehensive diagnosis of causes of impacts as suggested, e.g. in WFD Annex II is relatively rare [5]. To support end-users in applying the novel approaches, RiBaTox provides a decision tree and fact sheets on methods that end-users can apply. The idea for stepwise guidance to most-profitable approaches helps in the selection of methods from the available options. For example, for a local or regional diagnosis of the role of chemical pollution in affecting water quality in the European context (WFD Annex II) or for the design of monitoring approaches (WFD Annex V). The latter is illustrated in Table 1.

The full set of current fact sheets is shown in Additional file 1. Fact sheets contain contact information, so that end-users can contact scholars for more information on use and implementation or on novel developments of the methods, if needed.

END-USER EVALUATION

The RiBaTox web tool is one of the three major achievements of the recent research activities, next to the conceptual framework for solution-focused risk assessment and the provision of a strategy and a database to support management planning. RiBaTox collates the final results of the research in a user-oriented format, but as yet no extensive practice validation of its utility in case studies was feasible. It is clear, however, that the gaps between diverse chemical pollution cases, diverse diagnostic methods and diverse stakeholders need to be bridged. However, positive evaluations on the concept and approaches of RiBaTox have been received in both the planning phase (from the EU as commissioning body) and on the final product (the web tool). The latter was apparent from a dedicated stakeholder meeting in Paris, 2018, and from a memorandum of members of the stakeholder board [19]. This result can be understood in the context of 11 RiBaTox-dedicated stakeholder interactions, three dedicated RiBaTox surveys on draft web tools and the workshop with water managers, co-hosted together with stakeholder board member Veolia, June 2018.

Table 1: Illustration representing some elements of the RiBaTox decision tree and fact sheets, in relation to the conceptual framework for solution-focused risk assessment and end-user needs

DECISION TREE-LEVEL 1	LEVEL 2	LEVEL 3
MONITORING STRATEGIES		
	Sampling strategies	**Grab sampling** **Passive sampling for organic contaminants** **Passive sampling for trace metals** **LVSPE** **Event sampling**
	Analytical strategies	**Target analysis** **SOPs compounds** **SOPs compound classes** **Preparation of standards** **Suspect screening** **Non-target screening**
	Strategies for effect-based monitoring	**In vivo tools** **Benchmarks and trigger values** **Biological early warning systems**
	Strategies for toxicant identification	**Ecotoxicological mass balances** **Virtual EDA** **Higher tier EDA**
	Strategies for ecological assessment	**Macrofauna community based** **PICT** **Fish biomarkers** **Weight of evidence approaches**

The table shows a part of the decision tree that users are offered regarding monitoring strategies (column 1, WFD, Annex V). Column 2 shows the systematic sub-grouping of main actions that can be applied. Column 3 identifies specific techniques and provides detailed fact sheets

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at https://doi.org/10.1186/s12302-019-0244-7.

Additional file 1. RiBaTox fact.

Abbreviations
NORMAN: Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances; RiBaTox: Web tool on River Basin Specific Toxicants; WFD: Water Framework Directive.

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SOLUTIONS RECOMMENDS BETTER COORDINATION ACROSS EUROPEAN CHEMICALS LEGISLATION TO IMPROVE PROTECTION FROM EXPOSURE OF THE AQUATIC ENVIRONMENT TO POLLUTANT MIXTURES

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. 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.

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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 Products 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

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.

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at *https://doi.org/10.1186/s12302-019-0245-6*.

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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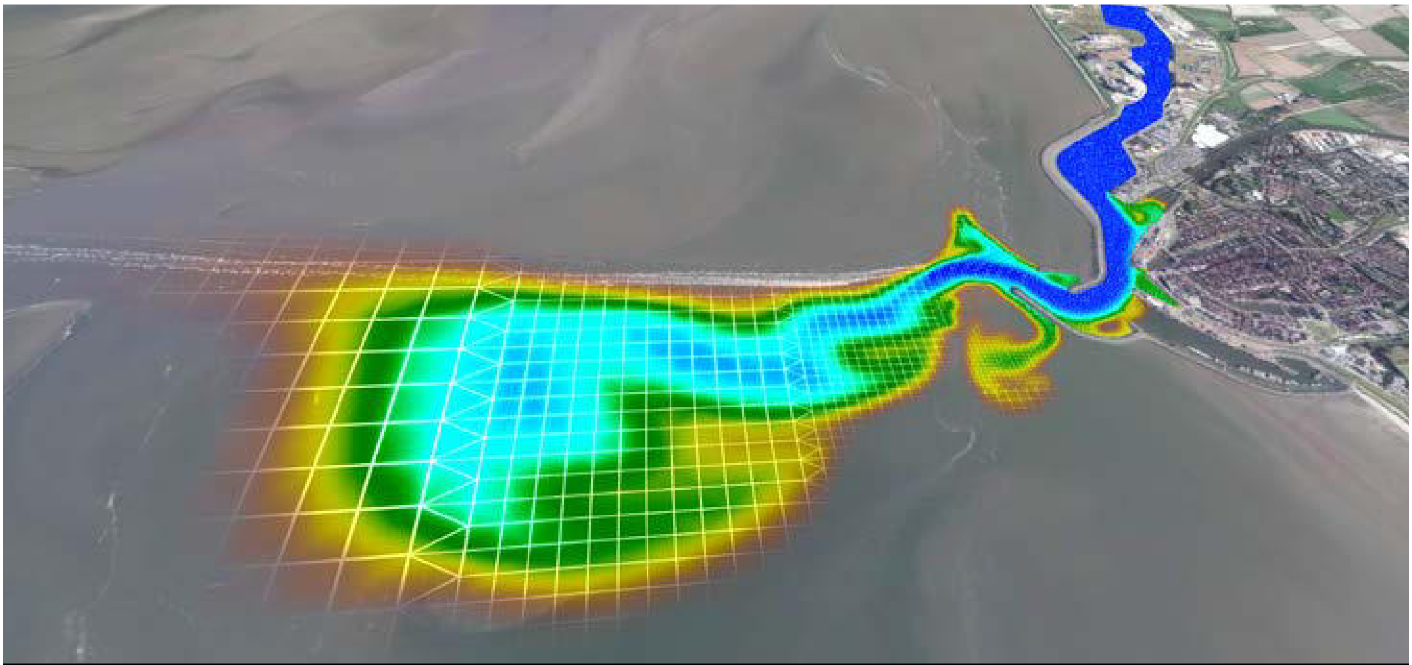
POLICY BRIEF



SOLUTIONS MODELS TO PROVIDE DIAGNOSTIC AND PROGNOSTIC CAPACITY AND FILL DATA GAPS FOR CHEMICALS OF EMERGING CONCERN

ABSTRACT

Water quality monitoring may give an incomplete picture of chemicals' contamination, due to the limited number of monitoring stations, samples and substances. Information gaps thus limit the possibilities to protect against and effectively manage chemicals in aquatic ecosystems. The SOLUTIONS project has developed and validated a collection of integrated models ("Model Train") to increase our understanding of issues related to emerging chemicals in Europe's river basins and to complement information and knowledge derived from field data. Unlike pre-existing models, the Model Train is suitable to model mixtures of thousands of chemicals, to better approach a "real-life" mixture exposure situation. It can also be used to model new chemicals at a stage where not much is known about them. The application of these models on a European scale provides temporally and spatially variable concentration data to fill gaps in the space, time and substance domains left open by water quality monitoring, and it provides homogeneous data across Europe where water quality data from monitoring are missing. Thus, it helps to avoid overlooking candidate chemicals and possible hot spots for management intervention. The application of the SOLUTIONS Model Train on a European scale presents a relevant line of evidence for water system level prognostic and diagnostic impact assessment related to chemical pollution.
The application supports the design of cost-effective programmes of measures by helping to identify the most affected sites and the responsible substances, by evaluating alternative abatement options and by exploring the consequences of future trends.

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CHALLENGE

More than 147,000 chemicals are registered under European Union legislative frameworks [1]. Analysis of surface water samples reveals the presence of many thousands of these chemicals in European rivers. Water Framework Directive (WFD) [2] compliant management requires a diagnosis of the likelihood that chemicals negatively affect the ecological status of surface waters or human health. When and where necessary, effective measures should be taken to reach the goal of good ecological status. Water quality monitoring gives an incomplete picture of chemical contamination due to the limited number of monitoring stations, of samples taken and analysed and of chemicals considered. These gaps in the space, time and substance domains limit the possibilities to protect against and effectively manage chemicals in aquatic ecosystems, since relevant chemicals may be overlooked, and hotspots or concentration peaks may go undetected. As monitoring programmes are designed at a river basin or sub-basin scale, inter-comparability across regions or across the EU can be improved. The high and ever-increasing number of chemicals on the market implies that protection and assessment approaches can no longer rely on substance-specific expert investigations only.

RECOMMENDATIONS

The modelling studies carried out in the EU FP7 project SOLUTIONS identified several applications of exposure and risk models that may substantially support monitoring and impact assessment. Thus, we recommend using models and their outcome.

- To complement water quality protection, assessment and management under the WFD to fill knowledge gaps on mixture risks and identify priorities for monitoring and management. This provides a more complete image of the likelihood of adverse effects on aquatic ecosystems and human health, both prospectively and retrospectively [3]. The SOLUTIONS project provides a consistent and integrated set of emission, exposure and effect models to achieve this goal, tested on the European scale.
- To support the assessment of chemical pollution threats. These provide consistent, spatially and temporally variable, Europe-wide estimates of the concentration of chemicals produced and used in Europe as well as risk estimates on aquatic ecosystems and on human health.
- To identify possible hotspots that would have been overlooked by chemical-safety assessment and/or using monitoring data alone.
- To identify potentially hazardous candidate chemicals for monitoring and management intervention that are missing in the current monitoring programmes.
- To use the hydrological relationships that make up water systems to better understand how upstream sources affect downstream receptors, in support to designing cost-effective remediation solutions.
- To better understand how the interplay of socioeconomic trends and policies (“Drivers”) influences the emissions of a wide range of chemicals and future emerging pollutants (“Pressures”), their occurrence in aquatic ecosystems (“Status”) and subsequent effects (“Impact”), substantiating the DPSIR-causal framework.
- To extend the chemical safety assessment for the authorization of chemicals [4] to provide a realistic estimate of the concentrations expected in EU River Basins, and the subsequent stress on aquatic communities and human health, and thus separate the probably harmless from the possibly harmful compounds.
- To explore the use of “big data”, automatic acquisition and processing protocols to address larger groups of chemicals.

REQUIREMENTS

- Modelling-based assessment and management relies on access to data on chemical production, emissions, fate and (eco-)toxicity and thus on maximum transparency.
- The use volume of a chemical is the key to reliably estimate in-stream concentrations (unless the chemical is only used in ways that do not lead to environmental losses). Especially for pharmaceuticals and pesticides, there are strong differences between (sub-)basins in the use volumes of individual chemicals. River basin managers, therefore, need access to information about the actual use volume of chemicals in the basin under their jurisdiction, regardless of commercial interests to keep such information confidential.
- Similarly, toxicity data for as many chemicals as possible are required. This asks for accessibility and transparency of data from chemical authorization and REACH dossiers, including the methodology through which they were established.
- Developments in society (e.g. changes in technologies and demographic change) affect pressures exerted by the presence of chemicals. For several developments and important groups of chemicals quantitative trend indications can be used in modelling to get a robust indication for future patterns of pollutants.
- An essential element of any spatially and temporally resolved model exercise is a good hydrology model, that provides reliable estimates of runoff and shallow groundwater flows. In SOLUTIONS we used the E-Hype hydrological model (by SMHI, Sweden). This model proved to be adequate for EU-wide assessments. For individual European river basins, the suitability needs to be confirmed.

- For further refinement of modelling more research is needed to predict the partitioning and degradability of "difficult" organic substances including volatiles, cations and zwitterions, to bridge toxicity data gaps and to model the interaction of chemicals with nonchemical stressors in ecosystems.

ACHIEVEMENTS

DEVELOPMENT OF THE MODEL TRAIN

The SOLUTIONS Model Train (SMT) consists of four building blocks: (a) simulation of emissions [5], (b) simulation of fate and transport [6] (c) characterisation of the mixtures' risk for aquatic ecosystems [7], and (d) the prediction of substance properties based on their molecular structure [8]. SMT simulates the emissions, fate and transport, and mixture toxic pressure as a function of space and time, related to the variability of weather, hydrology, wastewater management infrastructure, etc. The model provides fully quantitative outputs, i.e. spatiotemporal data on exposure and on the magnitude of risk (mixture toxic pressure). SMT operates on the scale of Europe or for individual European river basins. The spatial schematisation as well as the hydrology, temperature, soil type, land use and crop cover are derived from the pre-existing Europe-wide hydrology model E-Hype [9]. The model domain for Europe-wide simulations includes 22,728 sub-catchments, with an average size of 252 km^2 (Fig. 1).

CONCENTRATIONS OF CHEMICALS AND STRESS ON AQUATIC SYSTEMS ON EU SCALE

After a smaller scale exercise for pharmaceuticals in Sweden [10], we calculated the emissions and concentrations of 1785 chemicals on the scale of the EU. Figure 1 shows the computational domain, consisting of all river basins covering parts of the 28 EU countries, Norway and Switzerland. Figure 2 shows an example of the simulated emissions to surface waters of the pharmaceutical Fluconazole (CAS 86386-73-4; one of the 1785 chemicals). Figure 3 shows an example of the simulated concentrations in surface waters of the same chemical. The 1785 simulated chemicals include 1348 chemicals of various uses, extracted from REACH registration dossiers, 105 pharmaceuticals and 332 pesticides. They are a subset of 5100 chemicals with quantified emissions, for which sufficient degradability [11] and toxicity data [7] are already available. In addition, the mixture toxic pressure of these 1785 chemicals on aquatic communities was derived from simulated time-variable bioavailable concentrations. The result was converted to one overall map showing a classification of the mixture toxic pressure to diagnose sites with probably insufficient protection in line with Water Framework Directive guiding principles (Fig. 4). Note that for the remaining 3315 chemicals, current Predicted Environmental Concentrations may serve to identify chemicals that possibly occur in high concentrations and need to be prioritised for toxicity assessment. This study only considered direct effects of chemical exposure to effect endpoints such as growth and reproduction. Specific effects, such as endocrine disruption, were not addressed.

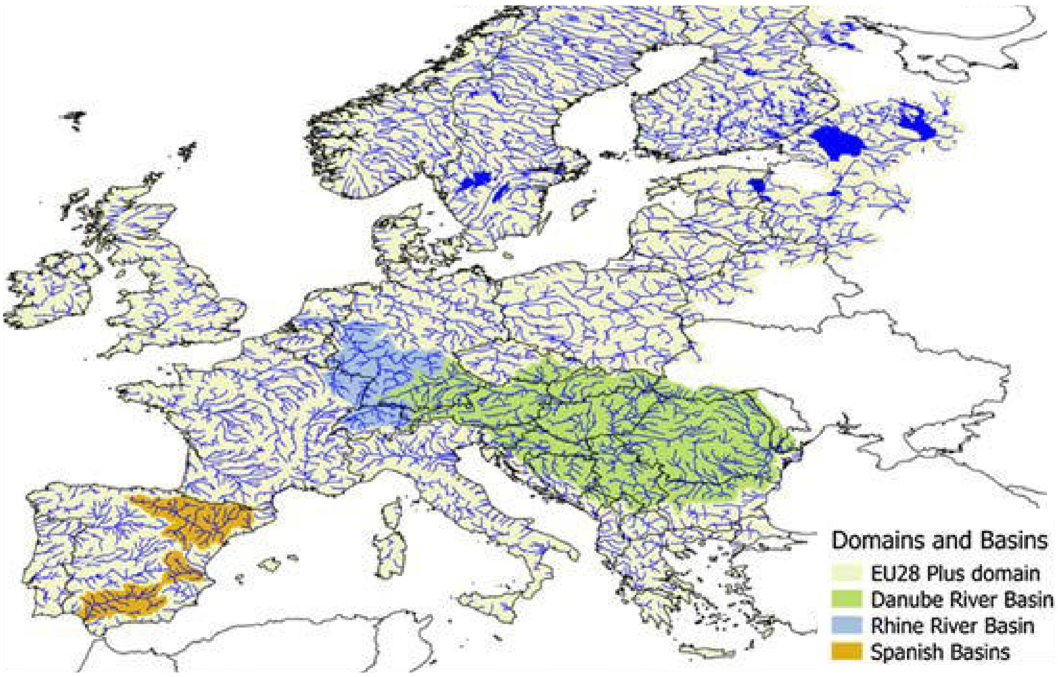

Fig. 1: SOLUTIONS modelling domain and case study areas for validation and demonstration

The validation of simulated concentrations [5] showed that their accuracy is not perfect, often associated to the limited availability of key input data (see "Requirements"). For 226 validation cases, the simulated concentrations were correct on average, with possible significant under- or overprediction for individual substances: for 65 % of cases the error was within one order of magnitude, while for 90 % of cases the error was within two orders of magnitude. This should be seen in a context of concentrations of chemicals spanning up to 16 orders of magnitude, and toxicity data spanning up to 9 orders of magnitude. Thus, the models can still provide a meaningful image of the expected impact, variable in space and time. The models can also cover a large number of substances. For these reasons, the models can supplement monitoring data for the diagnosis of current occurrence of and effects from chemicals and can provide a prognosis of the changes thereof as a result of socio-economic changes or the implementation of abatement measures. The below results illustrate this.

DIFFERENCES BETWEEN RIVER BASINS

The assessment of the model-derived data, both input and output, allowed for an analysis of differences between European river basins [12]. Which basins are the most affected? What factors are responsible? In a broad sense, the simulated chemicals' pressure in different river basins is determined by the pressure from population centres and economic activities (including agriculture and industry), relative to the dilution capacity of the surface water system. The highest effects are therefore encountered in relatively small river basins, if they happen to be highly developed and densely populated. An example of the latter is the Llobregat basin in Spain (≈ 5000 km^2, including the city of Barcelona).

ANALYSIS OF HOTSPOTS

The assessment of model-derived data also allows for an analysis of hotspots of high mixture toxic pressures— likely associated with high impacts on ecological status [see Policy Brief MARS-SOLUTIONS]—within river basins [12].

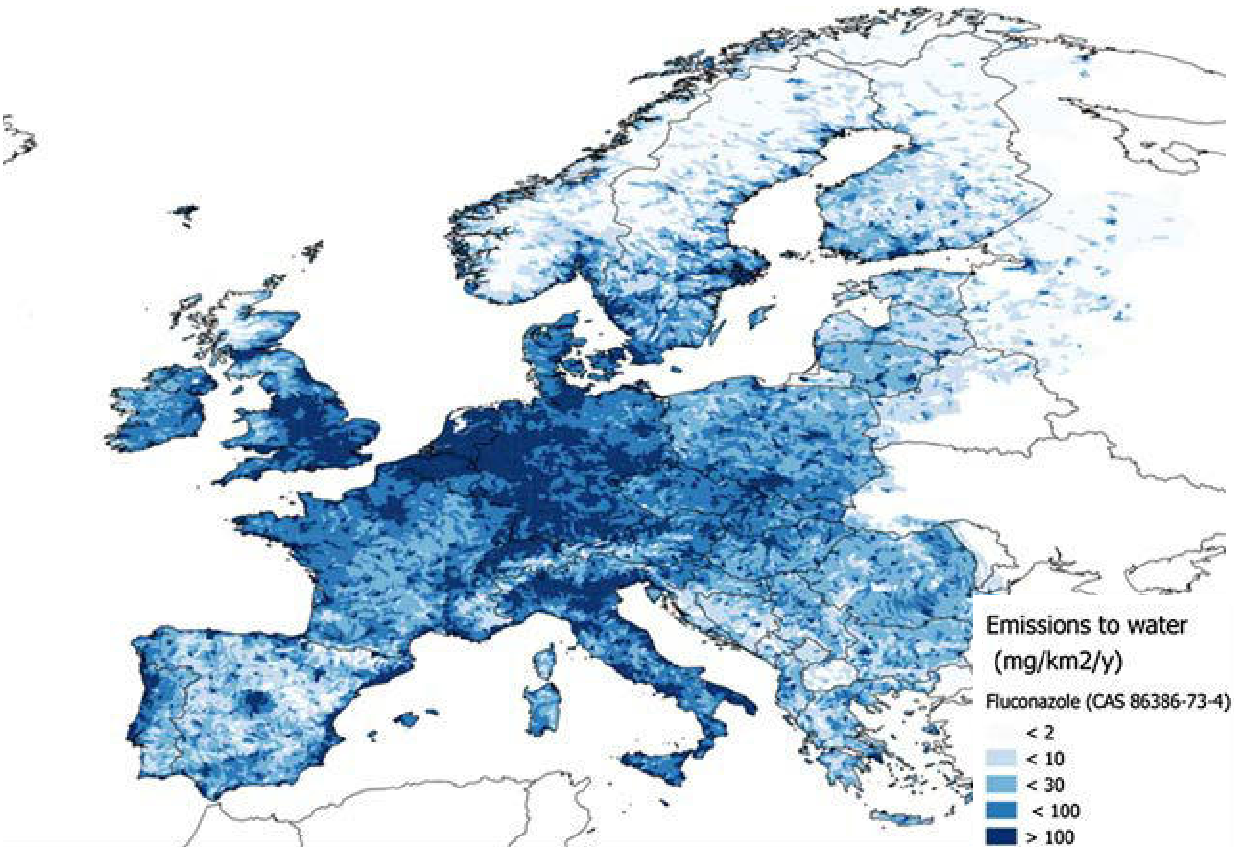

Fig. 2: Example of simulated emissions to surface waters of the pharmaceutical fluconazole (CAS 86386-73-4; one out of 1785 chemicals)

These hotspots are found in water systems of densely populated areas throughout Europe, such as Lisbon, Madrid, Valencia, Barcelona, Athens, the western part of the Netherlands, Essen-Dortmund, Brussels, Paris, St Petersburg and Belgrade.

RANKING OF SUBSTANCES

After model applications for individual substances (PFOS, PFOA, [13, 14]), toxic risks to aquatic ecosystems of 1785 chemicals produced in Europe have been simulated and potential drivers of mixture toxicity have been identified [12]. This exercise provided a spatially variable picture, especially for pharmaceuticals and pesticides, due to differences in the use intensity between EU countries. On a European scale, the substances expected to be the most relevant regarding ecological impacts via direct effects on vital traits such as growth and reproduction (out of the 1785 we analysed) were identified. Among these were the commercial chemicals octamethylcyclotetra- siloxane (CAS 556-67-2), dodecan-1-ol (CAS 112-53-8) and anthraquinone (CAS 84-65-1), as well as the fungicide chlorothalonil (CAS 1897-45-6). A similar assessment was done for different individual river basins.

On such smaller spatial scales, however, the results get more sensitive for the availability of reliable regional information about the use intensity of chemicals.

RANKING OF SITES AND SUBSTANCES IN A CONTEXT OF UNCERTAINTY

Sites and substance ranking based on predicted environmental concentrations (PECs) is sensitive to details of the methodology applied and to the uncertainty of the PECs. Ranking based on measured environmental concentrations (MECs) is sensitive to the available sampling stations and sampling times and to the accuracy of the laboratory analytical methods. Both approaches are sensitive to the method and data used for toxicity evaluation of the studied compounds. Consequently, sites and substances cannot and should not be ranked in absolute terms but can be classified, for example in a traffic light fashion:

- Site or substance is expected to present a risk (“red”)
- Site or substance is not expected to present a risk (“green”)
- Site or substance cannot be classified in the above categories (“yellow”).

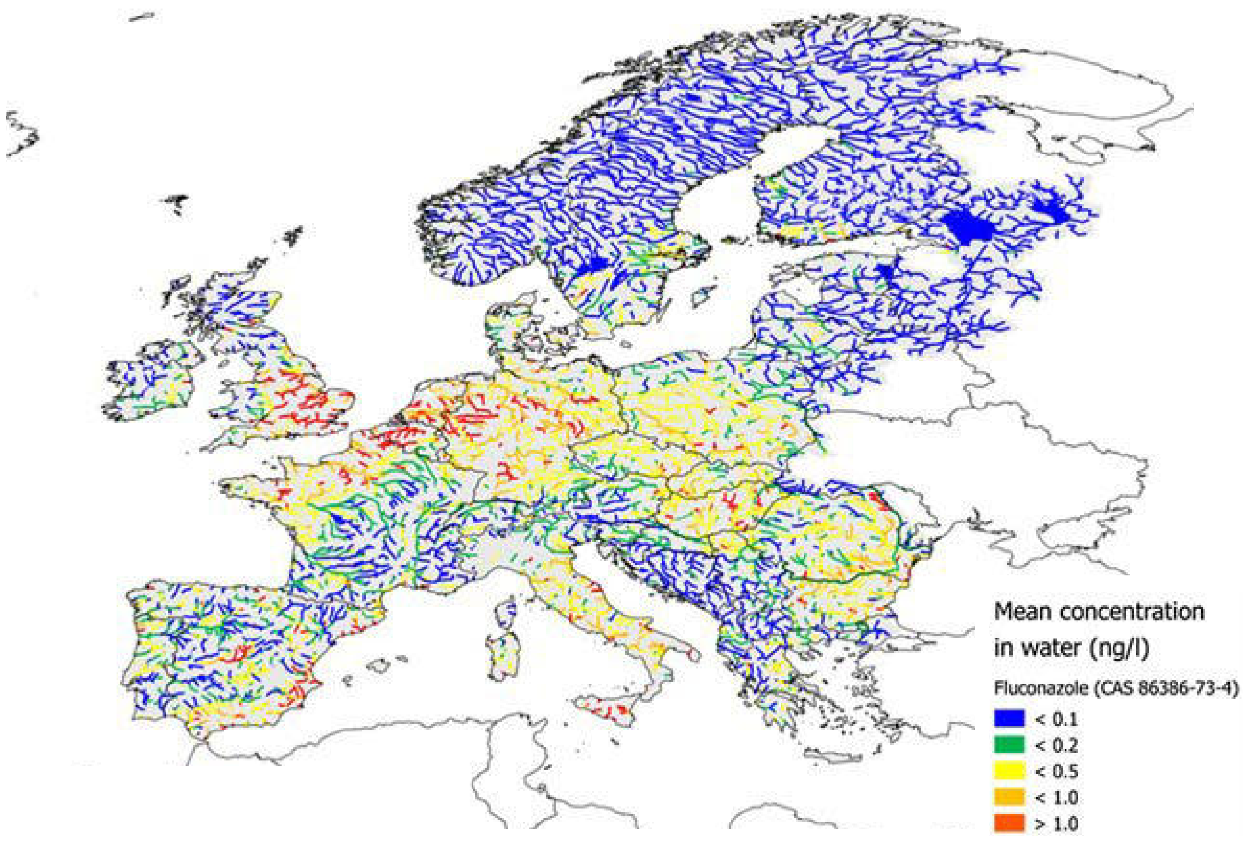

Fig. 3: Example of simulated concentrations in surface waters of the pharmaceutical fluconazole (CAS 86386-73-4; one out of 1785 chemicals)

The latter group needs more information to arrive at a conclusion, while they can still be ranked according to the likeliness to be “red” or “green”.

COST-EFFECTIVE ABATEMENT

The SOLUTIONS approaches and models have been used to test the efficacy of end-of-pipe measures in the wastewater chain to alleviate effects in surface waters [15, 16]. We demonstrated this in the Rhine Basin Case Study, first by evaluating the changes brought about by extra wastewater treatment throughout the basin, to evaluate the potential effect of such measures. By limiting the end-of-pipe measures to those sources with the highest contribution to the effects, a higher returnon- investment can be expected. In one example, about 70 % of the maximum reduction of mixture toxic pressure was achieved by extra treatment of only 20 % of the emission sources. Such a high return-on-investment was found only if a spatially differentiated water quality improvement was pursued: for example, improvement only in areas where drinking water is abstracted, or only at the basin outlet to protect the receiving marine waters.

FUTURE SCENARIOS

The SOLUTIONS models have been used to investigate the effects of expected trends in the use of chemicals towards the year 2030. One of such trends is the expected increased use of pharmaceuticals because of the ageing of the population. Based on the assumptions made, the simulation results indicated that the pressure from this substance group would increase by 36 % [8]. The scenario simulations also pointed out that the phasing out of substances of very high concern (SVHC), listed on the REACH Candidate List, can have a strong positive effect on water quality, whilst regrettable substitution (substitution by equally harmful substances) can be identified via modelling, and therefore, avoided. Candidate List substances include important groups of chemicals (e.g. plasticisers). The results show that regulation can have a high impact on the reduction of emissions of problematic chemicals [17] and is an important element for the transition to a more sustainable chemistry [18].

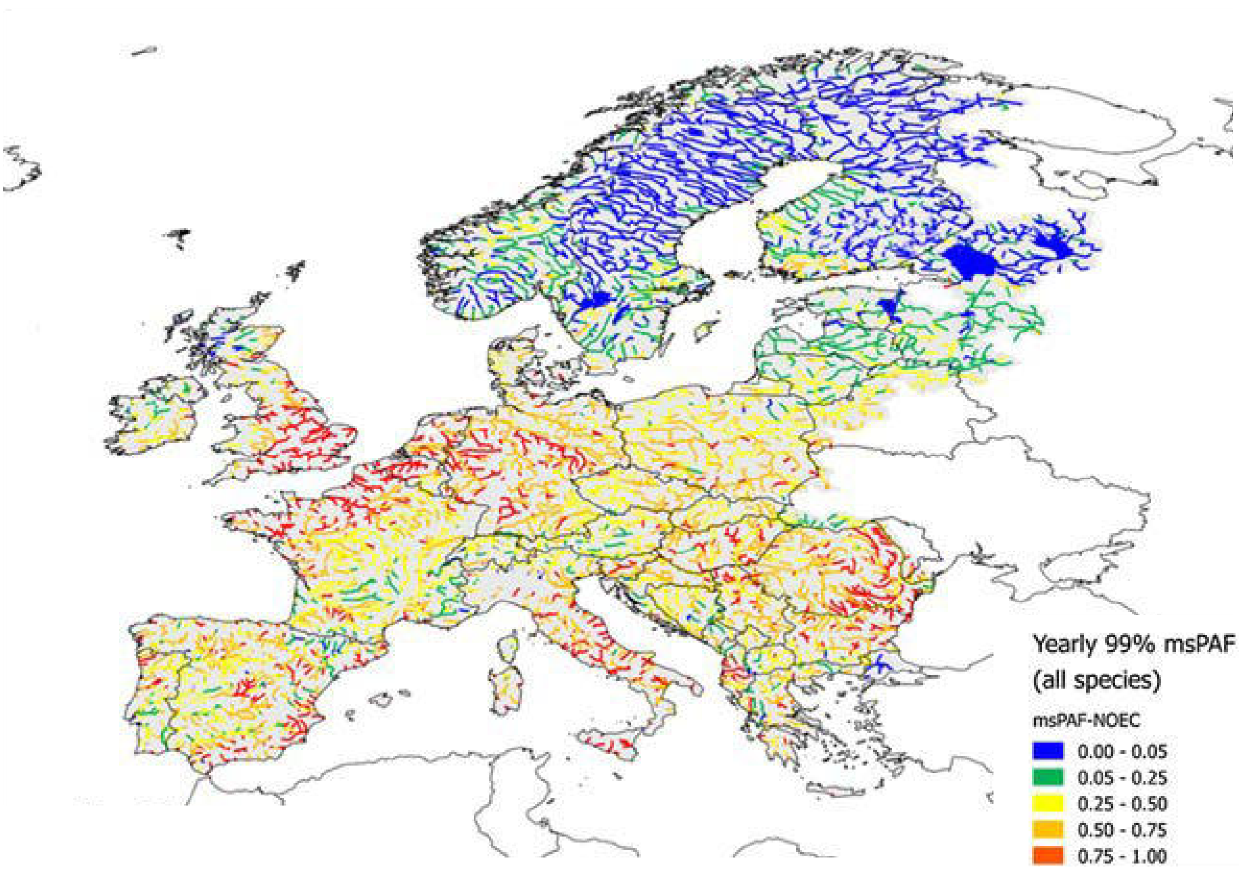

Fig. 4: Classification of level of protection against mixture effects derived from simulated time-variable, bioavailable concentrations of 1785 chemicals. Expected effects are quantified using the multi-substance potentially affected fraction of species (msPAF) derived from species sensitivity distribution effect model, based on no-observed effect concentration endpoint (SSD-NOECs))

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at *https://doi.org/10.1186/s12302-019-0248-3*.

Abbreviations

CAS: Chemical Abstracts Service (system for identification of chemicals); DPSIR: drivers, pressure, status, impact and response; a causal framework for describing the interactions between society and the environment, adopted by the European Environment Agency; EC50: effect concentration causing 50 % effect; MEC: measured environmental concentration; msPAF: multi-substance potentially affected fraction of species; NOEC: no effect concentration; PEC: predicted environmental concentration; PFOS: perfluorooctanesulfonate; PFOA: perfluorooctanoic acid; REACH: registration, evaluation, authorisation and restriction of chemicals; SSD: species sensitivity distribution; SVHC: substances of very high concern; WFD: Water Framework Directive.

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A METHODOLOGICAL FRAMEWORK FOR THE INTEGRATION OF MIXTURE RISK ASSESSMENTS INTO PRIORITISATION PROCEDURES UNDER THE EUROPEAN WATER FRAMEWORK DIRECTIVE

ABSTRACT

Current prioritisation procedures under the EU Water Framework Directive (WFD) do not account for risks from chemical mixtures. SOLUTIONS proposes a multiple-lines-of-evidence approach to tackle the problem effectively. The approach merges all available evidence from co-exposure modelling, chemical monitoring, effect-based monitoring, and ecological monitoring.
Full implementation of the proposed methodology requires changes in the legal text in adaptation to scientific progress.

CHALLENGE

As a strategy against chemical pollution, Article 16 of the EU Water Framework Directive (WFD) [1] requires the identification of EU-wide priority substances (PS) selected amongst those pollutants or groups of pollutants presenting significant risks to or via the aquatic environment. In addition, EU Member States are required to identify river-basin specific pollutants (RBSP) (WFD Article 4 and Annex V). Furthermore, beyond the fulfilment of EU-wide WFD requirements, national or regional rules and provisions may require local water managers to identify site-specific pollutants or groups of pollutants causing significant local risks. EU-wide priority substances, RBSPs, and site-specific pollutants are subject to risk reduction efforts. The aim is to reduce pollution to safe concentration levels, currently formatted as so-called environmental quality standards (EQS) for separate chemicals.
Current regulatory procedures for prioritisation [2–4] and EQS setting [5] are focused on single substances. Individual pollutants are assessed as if they would occur in isolation. The fact that they are part of complex multiconstituent mixtures is largely ignored. However, a mixture of pollutants usually poses a higher risk than each individual constituent alone, as detailed in a separate policy brief on mixture risks [6]. As a consequence, compliance with EQS values for single pollutants (PS and RBSP) may not be sufficiently protective against toxic effects from combined exposure to multiple chemicals. This is not just a theoretical assumption but has also been demonstrated empirically in a study led by the European Commission's Joint Research Centre [7].
The problem is well recognized but approaches for tackling it effectively were missing. The EU project SOLUTIONS, therefore, took up the challenging task to develop a proposal for an advanced methodological framework which integrates mixture risk assessments into prioritisation procedures under the WFD. The prioritisation is important to make river basin management planning most efficient.

RECOMMENDATIONS

SOLUTIONS proposes a multiple lines-of-evidence (LOE) approach for the identification of priority mixtures presenting significant risks and drivers of mixture toxicity dominating the overall risks (Fig. 1). The suggested methodology is applicable at all scales (EU, river basin, and site-specific level).

The approach merges evidence from

- **i.** chemical monitoring, in combination with socalled component-based approaches for mixture risk assessment and driver identification,
- **ii.** integrated modelling of co-exposure and resulting mixture risks,
- **iii**. effect-based monitoring, in combination with socalled effect-directed analyses or related methods for the identification of causative (groups of) pollutants,
- **iv.** ecological monitoring, (field observations on socalled biological quality elements), in combination with possible indications on causative (groups of) pollutants.

The multiple LOE approach is detailed in a public SOLUTIONS deliverable [8]. Explanations of individual techniques are given in dedicated policy briefs on chemical screening [9] and associated component-based methods [10], modelling of co-exposures [11] and resulting mixture risks [6], effect-based methods [12], and ecological tools [13].
For developing the approach, SOLUTIONS thoroughly examined all available concepts and methods for both (i) the regulatory assessment of risks from chemical mixtures and (ii) the integration of such mixture risk assessment methods into prioritization procedures. No single method was found to provide a comprehensive solution for the complex problem of assessing risks from pollutant mixtures in the aquatic environment. Every option has some advantages but also suffers from specific limitations. As the best possible way forward, SOLUTIONS, therefore, proposes a framework which integrates all available LOEs on significant risks.
The advanced framework does not replace existing procedures for single substance prioritisation but integrates them with novel methodological elements into the suggested multiple LOE approach. Where one or more lines of evidence identify groups of pollutants presenting a significant risk, these should be included in ranking procedures for risk reduction measures. Criteria for mixture risk ranking may be essentially the same as those which have been established for single substance prioritization, including the frequency and the extent of threshold exceedances [14]. Where appropriate, large groups of dozens or hundreds of Fig. 1 co-occurring pollutants may be reduced to few mixture components or even one single component which can be demonstrated to explain most of the overall risk, socalled drivers of mixture risks.
Wherever conclusive evidence on significant risks and resulting needs for risk reduction cannot be provided because all LOEs suffer from significant knowledge-gaps, mixture components of potential concern are not left unaccounted for but are prioritised for further research and testing. This principle is adopted from the NORMAN approach for the prioritisation of individual substances of emerging concern [15].

IMPLEMENTATION

Implementation of the proposed framework for effectively dealing with mixture risks under the WFD requires changes in the legal text. The following is needed:

- A broader approach to the prioritisation of pollutants for risk reduction measures, including all substances that make a significant contribution to an unacceptable overall risk, irrespective of whether they exceed individually acceptable levels or not.
- Comprehensive assessments of the chemical status, including all pollutants at a given site. Currently, EU wide priority substances and RBSPs are assessed in isolation. EU wide priority substances define the “chemical status”, while RBSPs are considered to affect the “ecological status”. In a real water sample, however, both types of pollutants occur together and they may be accompanied by site-specific pollutants. EU wide priority pollutants, RBSPs, and site-specific pollutants jointly contribute to the overall mixture risk. Therefore, they need to be assessed together.
- Uniform legal principles and harmonised technical rules for the assessment and prioritisation of pollutants and pollutant mixtures on different scales such as EU wide priority substances, RBSPs, and sitespecific pollutants. For example, EQSs or PNECs or other reference values used by different Member States for RBSP identification currently differ, sometimes by orders of magnitude [16]. Such inconsistencies in single substance assessments render transparent, consistent, and meaningful mixture risk assessments impossible.
- A clear legal mandate for the establishment of an effect-based monitoring system, which may be performed in parallel to chemical monitoring or which may serve as a trigger for targeted chemical monitoring, as detailed in a European technical report [17] and specifically addressed in a separate Policy Brief [12].

These special needs for amendments are part of a broader array of recommendations for revising the WFD with the aim to improve the achievement of its protection and risk reduction goals, as detailed in Brack et al. [18].
Chemical risk assessment and risk-based prioritisation are data-hungry exercises. The generation of necessary input data, however, is not part of the WFD but governed by other pieces of EU chemicals legislation. In addition to amending the WFD, complementary measures must, therefore, be taken to ensure data availability. Currently, the limited availability of (eco)toxicity data that are considered reliable for EQS derivation already poses a serious problem for the assessment of many individual water pollutants. For conclusive mixture risk assessments, the lack of such single substance toxicity data is an even more severe bottleneck [6]. In addition, co-exposure modelling suffers from the limited availability of chemical use and emission data [11]. The WFD does not include mechanisms to close any of these data gaps. Strengthening risk assessments of both individual aquatic pollutants and pollutant mixtures, therefore, requires cross-cutting initiatives, including all pieces of EU chemicals legislation [19] and clearly assigning responsibilities for providing reliable (eco)toxicity data.

Fig. 1: Graphical presentation of the proposed multiple lines-of-evidence approach for the identification of priority substances and priority mixtures under the EU Water Framework Directive

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at https://doi.org/10.1186/s12302-019-0239-4.

Abbreviations

EQS: environmental quality standards; LOE: lines-of-evidence; PS: priority substances (in the sense of the WFD); RBSP: river-basin specific pollutants; WFD: Water Framework Directive.

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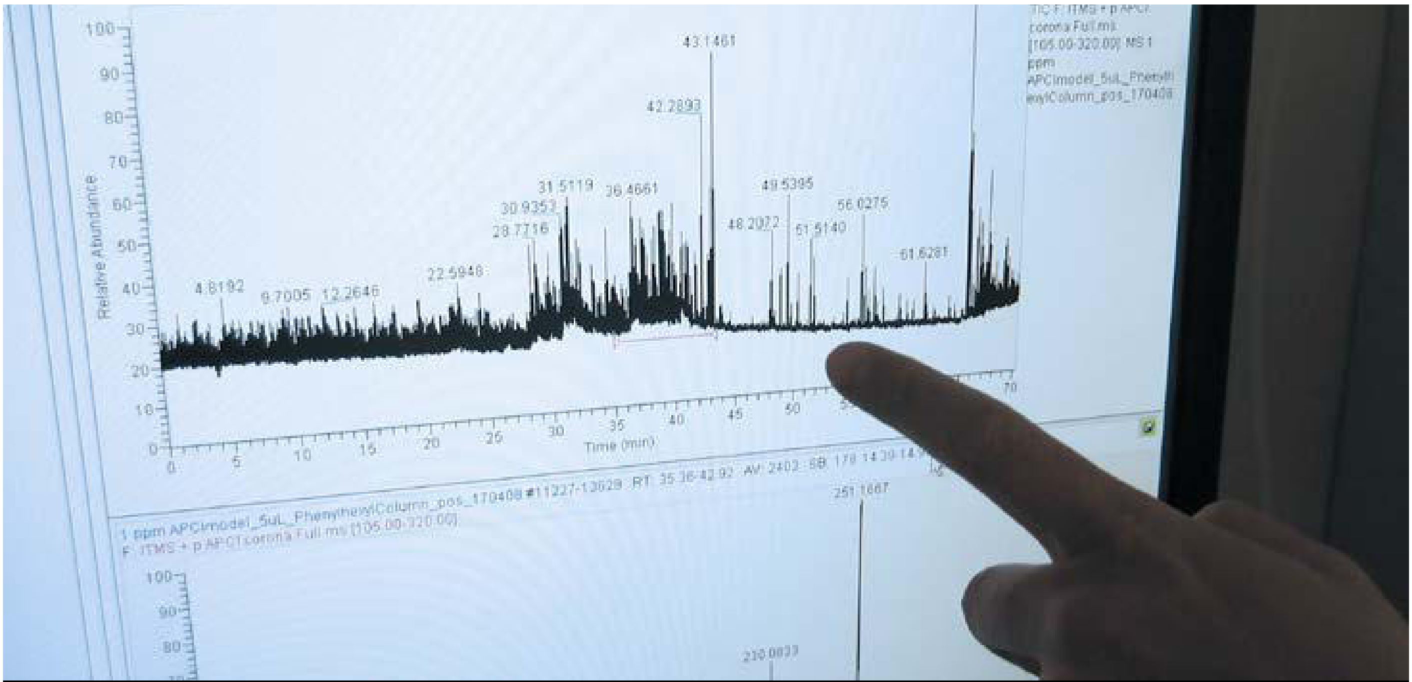

HIGH-RESOLUTION MASS SPECTROMETRY TO COMPLEMENT MONITORING AND TRACK EMERGING CHEMICALS AND POLLUTION TRENDS IN EUROPEAN WATER RESOURCES

ABSTRACT

Currently, chemical monitoring based on priority substances fails to consider the majority of known environmental micropollutants not to mention the unexpected and unknown chemicals that may contribute to the toxic risk of complex mixtures present in the environment. Complementing component- and effect-based monitoring with widescope target, suspect, and non-target screening (NTS) based on high-resolution mass spectrometry (HRMS) data is recommended to support environmental impact and risk assessment. This will allow for detection of newly emerging compounds and transformation products, retrospective monitoring efforts, and the identification of possible drivers of toxicity by correlation with effects or modelling of expected effects for future and abatement scenarios. HRMS is becoming increasingly available in many laboratories. Thus, the time is right to establish and harmonize screening methods, train staff, and record HRMS data for samples from regular monitoring events and surveys. This will strongly enhance the value of chemical monitoring data for evaluating complex chemical pollution problems, at limited additional costs. Collaboration and data exchange on a European-to-global scale is essential to maximize the benefit of chemical screening. Freely accessible data platforms, inter-laboratory trials, and the involvement of international partners and networks are recommended.

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CHALLENGE

Chemical monitoring according to the European Water Framework Directive (WFD) [1] currently addresses 45 priority substances (PS) [2] to establish the chemical status together with different sets of nationally defined River Basin Specific Pollutants (RBSP). Approximately 300 RBSPs are considered (in total) across the different EU Member States. However, this selection only reflects a very small fraction of all chemicals that may occur in European water bodies [3]. Recently, complementing PS and RBSP component-based monitoring with the application of effect-based methods (EBM) was suggested, to assess the likelihood that chemical contamination causes harm to human health or aquatic ecosystems, as well as to develop measures to reduce chemical pollution impacts [4]. This EBM approach will help to identify, detect, and quantify groups of chemicals affecting toxicological endpoints of concern and identify hot spots of toxic risks. However, neither WFD component nor effect-based monitoring and assessment in their current forms are able to detect, identify, and quantify individual chemicals of potential concern beyond PS and RBSPs, i.e., 99.8 % of the chemicals in commerce, and their mixtures. Thus, newly emerging chemicals, unexpected spills and chemicals with increasing concentrations remain unrecognized until toxicity thresholds are exceeded and an identification of the drivers of the measured effects for example using effect-directed analysis (EDA) [5] is triggered. Early warning of the emergence of new chemical threats would help to initiate efficient abatement even before EBMs indicate toxicity. At the same time, source identification is often the key for targeted abatement measures [6], but may be challenging without any information on the nature of the newly emerging chemicals in the water body of concern. Thus, the current status-related monitoring must be complemented with wide-scope target, suspect, and non-target screening (NTS) (Fig. 1), combined with component- and effect-based methods to protect against and assess the presence and risks of complex mixtures. This is the challenge that needs to be overcome on the way towards a more holistic and solution-oriented protection, monitoring, and assessment [7].
Powerful LC-HRMS- and GC-HRMS-based screening methods are increasingly available [8–12]. Thus, this paper wants to encourage monitoring practitioners, water managers, and policy makers to consider these new techniques to achieve a more holistic water quality assessment and to enhance awareness on the multifold potential to make abatement and management of water pollution more efficient.

RECOMMENDATIONS

- *Apply analytical screening wherever possible, to comprehensively assess chemical pollution beyond the PS and the RBSP.* Non-target screening (NTS) with state-of-the-art gas- and liquid-chromatography high resolution mass spectrometry (GC-HRMS and LCHRMS) is able to provide an increasingly comprehensive picture of the presence of dissolved chemicals in a water body strongly supported by rapidly developing automated data analysis workflows. This provides management-relevant information even if only a minority of the signals can be annotated with compound names. Management-relevant information from NTS can be gained in different ways:

  – *Screen NTS data for hundreds to thousands of known compounds* of possible concern using stateof- the-art computational workflows. This will greatly extend the list of chemicals monitored and potentially considered in future risk and impact assessments. Combining target screening with toxicity data [14] can be used to estimate the likelihood of impacts on the water quality status applying toxic units (TU) [15] or the multi-substance potentially affected fraction of aquatic organisms (msPAF) [14, 16].
  – *Use NTS data to establish source-related contamination fingerprints [7].* Fingerprints may be defined as combinations of NTS signals or compounds that are characteristic for specific domestic, industrial or agricultural activities. Identifying. them in surface waters will help understanding complex contamination patterns in surface waters not only as mixtures of individual compounds but as an overlay of source-related fingerprints with background signals and site-specific individual components. This will help to estimate, prioritize, and abate contributions of pollution sources.
  – *Screen NTS data for newly emerging signals,* signals with changing trends over space or time, which may indicate emerging chemical hazards even if the identity of chemicals involved is initially unknown [17]. This can be used to trigger efforts on compound and source identification and source-related abatement measures.
  – *Screen NTS data for ubiquitously occurring peaks* that might be of Europe-scale concern, as well as for rare and site-specific peaks that help to identify specific local sources of contamination for abatement measures [18]. Chemicals containing heteroatoms and halogens, often indicating anthropogenic and possibly toxic compounds, can be identified as well [8, 12, 19, 20].
  – *Use NTS for the identification of transformation products* for example in wastewater treatment plant effluents if applied together with knowledge on biotransformation reactions and multivariate statistics [21–23].

  - *Correlate NTS data with effect-based monitoring data* or ecological information to identify potential drivers of toxic impacts [24].

- *Harness this progress in chemical analysis and integrate NTS into ongoing WFD chemical monitoring activities*. Monitoring of many PS and RBSPs at concentrations below the Environmental Quality Standards (EQS) in many cases already applies modern LC-HRMS techniques. These techniques are becoming increasingly available in laboratories of water suppliers, monitoring stations and in commercial labs. Thus, complementing current analyses methods with NTS requires limited additional analytical efforts, but provides great opportunities to protect against, monitor, and manage so far unknown or unexpected contamination that affect the ecological status of surface waters or drinking water production.
- *Participate in international networks* that are advancing NTS and transferring this to policy, such as NORMAN (Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances, *https://www.norman-network.net)*, and benefit from collaborative trials that have been performed [25, 26].
- *Store NTS data in repositories for retrospective analysis and support open science for identifying emerging chemicals (See also [27])*. Freely available community database resources with high quality data are essential for data exploration via rapid retrospective screening for the temporal and spatial occurrence of newly identified compounds [28, 29]. Community support with curation of chemical structures and relevant information for suspect prioritization including compound properties, toxicity data, use information, production tonnages, and previous detections is encouraged [30]. NTS repositories will help to understand long-term trends of contamination even for compounds that are not currently monitored, so many parties can benefit from the rapidly improving analytical technology as well as from globally increasing data exchange.

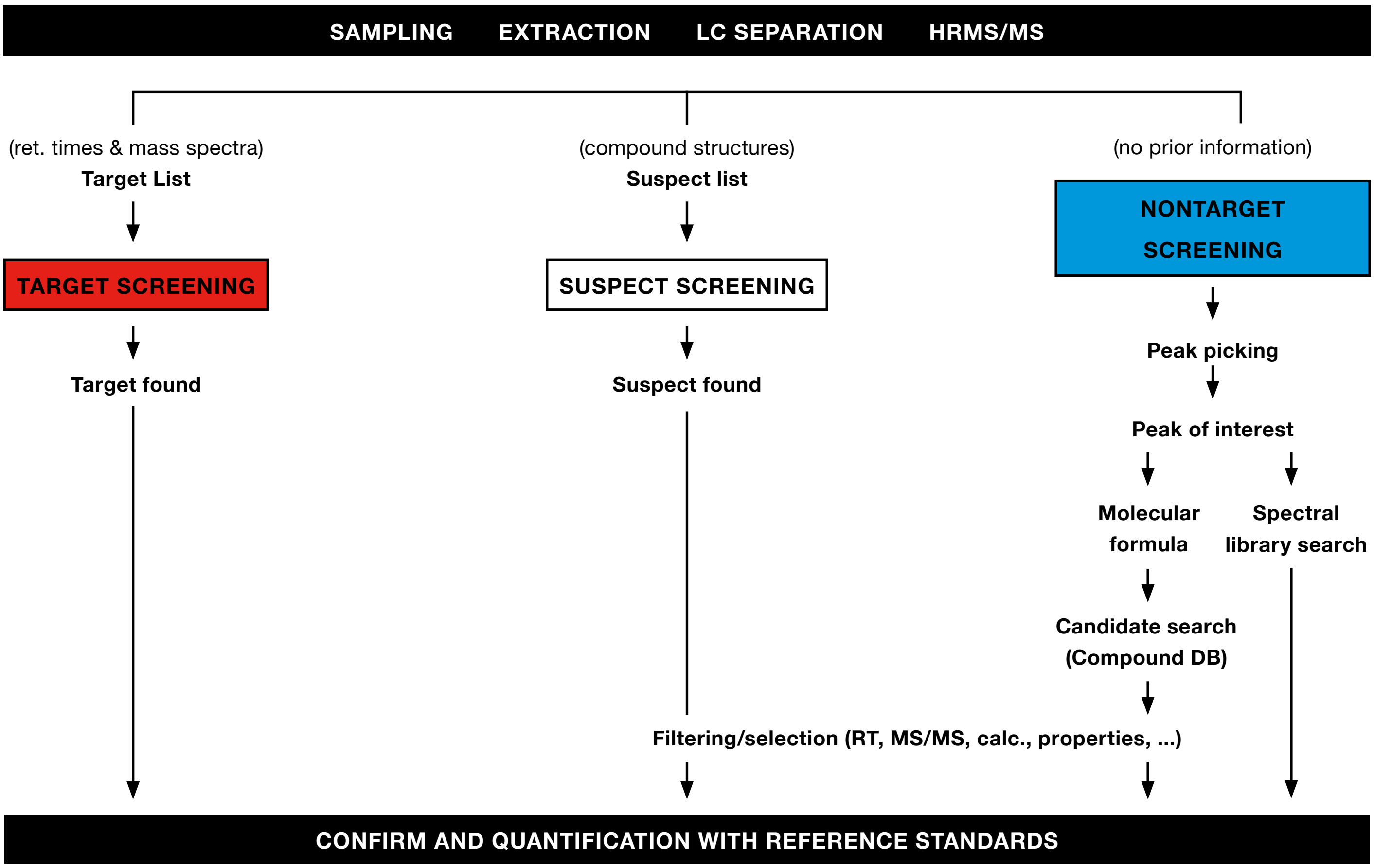

Fig. 1: Scheme of analytical screening addressing targets, suspects, and non-targets (modified after [13])

REQUIREMENTS

The technology for GC- and LC-HRMS based NTS is fit for purpose [17] and continuously advancing. Automated workflows for data evaluation are opening up this technology for routine monitoring. Front runners in official monitoring in many European Member States already perform NTS of European surface waters [17]. The largescale implementation requires a paradigm change with the:

- Awareness that chemical pollution is much more than a chemical and ecological status of a water body based on PS and various sets of RBSPs and the understanding that NTS of the entire mixture complemented with component and/or effect-based methods is essential for early warning of new contaminants, recognizing undesired trends in pollution, providing data for future retrospective assessment and for triggering cost-efficient management measures;
- Upgrade of existing laboratories with HRMS technology and the training of the staff in NTS to enable monitoring groups in all EU Member States to address complex chemical mixtures analytically. Learn from monitoring stations that are already routinely applying NTS for example at the River Rhine [17].
- Willingness of free data exchange and international collaboration. The establishment and/or continuing support of free data exchange platforms will strongly enhance the success rate of identification of compounds in the environment. This data exchange should involve scientists and regulators but also industry.
- Preparedness to further advance NTS and to develop criteria and procedures to evaluate quality criteria concerning accuracy, precision, sensitivity, and reproducibility to enhance acceptance and to maximize the benefit from application for assessment and management [31].

ACHIEVEMENTS

USING NTS FOR WIDE-SCOPE TARGET SCREENING

While traditional target analysis often addressed only a limited number of contaminants, NTS now allows an "all-in-one" measurement and data can be directly used for target screening of hundreds to thousands of chemicals in monitoring studies [32, 33]. Examples are the screening for about 270 and 400 target chemicals in order to evaluate the impact of non-treated and treated wastewater effluents on the micropollutant burden in water in the River Danube [34, 35] and in small streams in Switzerland [36], respectively. In these studies, linking target screening with effect-based monitoring [4] was shown to help assess toxic risks, identify drivers of toxicity, quantify their contribution to mixture risks, and indicate the risk that is not explained by the limited selection of current target chemicals. In a study on wastewater treatment plant (WWTP) effluents, target screening helped to unravel seasonal dynamics in organic pollutant mixtures and related toxic risks [37].

DEVELOPMENT AND ASSESSMENT OF AUTOMATED METHODS

for small molecule identification Software-based automated data processing methods play a critical role for the successful identification of compounds from NTS data. In general, NTS workflows start from detection of peaks by the peak picking software. To maximize the quality and number of detected peaks the performance of one of the widely used data processing software packages MZmine 2 was assessed for LCHRMS data [14] and validated on both spiked and real surface water samples. This optimization workflow for MZmine 2 can be applied to data from other LC-HRMS instruments.

In compound identification, in silico MS/MS fragmentation prediction approaches are most widely applied to assign a compound structure to an unknown peak. The evaluation of the Critical Assessment of Small Molecule Identification (CASMI) 2016 contest [38] showed a substantial improvement in (semi-)automated fragmentation methods for small molecule identification. The inclusion of metadata information (e.g., commercial relevance of compounds) further improves the identification success for "real life" annotations of environmental contaminants [39].

In another study, a data set of 78 diverse known micropollutants analyzed by LC-HRMS was used to assess two different MS/MS fragmentation and two retention prediction approaches. To combine scores from these different candidate selection tools, consensus score values with optimal weights were calculated to show the contribution of each approach and whether the combination could improve candidate selection [40, 41].

Automated small molecule identification approaches require reporting standards that reflect the confidence of the identification based on NTS data. The "Level system" proposed in [42] has been used in SOLUTIONS and NORMAN efforts for communicating NTS results [25].

NTS IN ROUTINE MONITORING — THE RIVER RHINE CASE STUDY

The international Rhine monitoring station has showcased the use of NTS with automated workflows in routine monitoring [17]. This involves the automated screening for 320 target compounds for long-term trend analysis, suspect screening of 1500 compounds to identify peak events and emission patterns, and NTS to detect accidental spills of previously undetected compounds. Daily trend analysis revealed peak signal intensities triggering compound identification efforts. In 2014, ten major spill events of previously undetected compounds were recorded, representing a chemical load of more than 25 tons in the River Rhine.

USE OF NTS TO IDENTIFY SITE-SPECIFIC POLLUTION

While the focus of chemical monitoring in Europe is on chemicals that are relevant on a European or basin scale, risks and impacts on water quality and ecosystems are quite often due to site-specific chemicals including many unexpected or unknown chemicals, which are typically overlooked or, in some cases, discovered via effect-based monitoring and identified by effect-directed analysis [24, 43]. Thus, an NTS-based approach has been developed and tested in case studies, which applies a rarity score based on detection frequency and ratios of maximum to median peak intensity on a set of sites of concern to identify water bodies with extensive occurrence of site-specific peaks [18]. Focusing identification efforts on these peaks allowed for the establishment of major sources of pollution that should be addressed by targeted abatement [6].

INTEGRATION OF NTS WITH MULTIVARIATE STATISTICS TO PRIORITIZE UNKNOWN TRANSFORMATION PRODUCTS

During wastewater treatment, about 50 % of parent micro-pollutants are (bio)transformed but not completely mineralized [44]. As a result, transformation products (TPs) are of major concern in environmental monitoring. NTS and parent/TP similarity has been used to identify TPs formed in wastewater treatment [22]. This approach combines principle component analysis (PCA) with difference analysis from known biotransformation pathways to prioritize NTS data and identify pairs of parent compounds and TPs. PCA and hierarchical clustering was also applied to prioritize TPs formed during ozonation of wastewater [21].

EXPLORING THE POTENTIAL OF A GLOBAL EMERGING CONTAMINANT EARLY WARNING NETWORK

Alygizakis [28] introduced a pilot study for a global emerging contaminant early warning network, led by NORMAN, and supported by SOLUTIONS. Eight reference laboratories used archived NTS data from a range of samples for subsequent retrospective screening of a list of new and emerging contaminants contributed by members (*https://comptox.epa.gov/dashboard/chemical_lists/normanews* and *https://zenodo.org/record/2623816*). This revealed the widespread occurrence of drug transformation products (e.g., gabapentin-lactam, metoprolol acid, and 10-hydroxy carbamazepine), several surfactants (e.g., polyethylene glycols), as well as industrial chemicals such as 3-nitrobenzenesulfonate and bisphenol S.

This Policy Brief highlights the opportunities of HRMS screening for a holistic monitoring and assessment of chemical pollution with limited additional efforts, accentuates the benefit of recording, compilation and exchange of NTS data for retrospective analysis to understand trends of pollution, even for compounds which are not in the focus today, and highlights the need for establishing open science, international collaboration, and data exchange to maximize the benefit for environmental assessment and protection.

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at *https://doi.org/10.1186/s12302-019-0230-0*.

Abbreviations
CASMI: critical assessment of small molecule identification; EBM: effect-based methods; EDA: effect-directed analysis; EQS: environmental quality standard; GC: gas chromatography; HRMS: high-resolution mass spectrometry; LC: liquid chromatography; NORMAN: network of reference laboratories, research centres and related organisations for monitoring of emerging substances; NTS: non-target screening; PCA: principle component analysis; PS: priority substances; RBSP: river basin-specific pollutants; TP: transformation product.

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POLICY BRIEF

STRENGTHEN THE EUROPEAN ENVIRONMENTAL RESEARCH TO MEET EUROPEAN POLICY GOALS FOR A SUSTAINABLE, NON-TOXIC ENVIRONMENT

ABSTRACT

To meet the United Nations (UN) sustainable development goals and the European Union (EU) strategy for a nontoxic environment, water resources and ecosystems management require cost-efficient solutions for prevailing complex contamination and multiple stressor exposures. Collaborative European research seems an ideal instrument to mobilize the required transdisciplinary scientific support and tackle the largescale dimension and develop options required for implementation of European policies. Calls for research on minimizing society's chemical footprints in the water–food–energy–security nexus are required. European research should be complemented with targeted national scientific funding to address specific transformation pathways and support the evaluation, demonstration and implementation of novel approaches on regional scales.

The foreseeable pressure developments due to demographic, economic and climate changes require solution-oriented thinking, focusing on the assessment of sustainable abatement options and transformation pathways rather than on status evaluation. Stakeholder involvement is a key success factor in collaborative projects as it allows capturing added value, to address other levels of complexity, and find smarter solutions by synthesizing scientific evidence, integrating governance issues, and addressing transition pathways. This increases the chances of closing the value chain by implementing novel solutions. For the water quality topic, the interacting European collaborative projects SOLUTIONS, MARS and GLOBAQUA and the NORMAN network provide best practice examples for successful applied collaborative research including multi-stakeholder involvement.

CHALLENGE

To achieve a sustainable development and maintain welfare, distinct sustainable development goals (SDG) are consented in international policy *(https://www.un.org/sustainabledevelopment/sustainable-development-goals/)*. The implementation of the SDG, however, faces enormous challenges at continental and global scales, including climate change [1], chemical pollution, urbanization and demographic changes [2], quantitative and qualitative shortage of freshwater for drinking water production and ecosystem functioning, and the loss of biodiversity and ecosystem services [3, 4]. Recently, the Background Report by the UN's Environment Assembly "Towards a pollution-free planet" estimated "19 million premature deaths annually as a result of the way we use natural resources and impact the environment to support global production and consumption" [5]. While chemical consumption and production are expected to double within the next 15 years [6], pesticides and other pollutants are reported to already pose significant risks to aquatic ecosystems [7] and compromise ecosystem biodiversity [8]. Environmental pollution, particularly pesticides, had been identified as drivers of the decline of insects and birds and thus compromise related ecosystem services such as pollination [9, 10]. Wildlife and humans experience lifelong continuous exposure to complex mixtures of chemicals in concert with other stressors [11]. This stands in contrast to established regulatory sectoral thinking that so far prevails in chemical safety and environmental protection, quality assessment and management. To foster sustainable chemistry development, the challenge is to overcome 'silo' thinking and to develop means to comprehensively understand, predict, and assess aggregated individual exposure (exposome) and stress profiles to identify the means for dealing with real-world complexity and dynamics. This perspective would allow new and original thinking about options to prevent and limit mixture risks and support sustainability in chemical use and land management.

The EU strategy for a non-toxic environment *(http://ec.europa.eu/environment/chemicals/non-toxic/index_en.htm)* responds to these challenges and provides an ambitious commitment in support of goals, geared towards the provision of food (SDG 2), clean water for humans (SDGs 3 and 6), responsible production and consumption (SDG 12), as well as safeguarding of aquatic life (SDG 14). Furthermore, as the SDGs are interconnected [12], integrated environmental policies and strategies are required to protect our natural capital, stimulate resource-efficient, low-carbon growth and innovation, safeguard people's health and well-being while respecting the Earth's natural limits [13].

Evidence-based approaches to support these strategic goals are needed. Current scientific knowledge, however, is often produced in fragmented settings based on disciplinary, small-scale studies that produce scientifically interesting results but with limited dissemination to decision makers. Moreover, since stakeholders are hardly, if ever, involved in basic research, many scientific findings remain unnoticed or are taken up for policy action only after decade-long delays [5]. Furthermore, there are limitations for national science funding schemes when it comes to large-scale multidisciplinary challenges such as understanding global processes, managing large ecosystems, e.g., river basins that cross national borders, or safeguarding environmental quality for multiple, often conflicting, purposes.

The scientific and technical means to record unparalleled amounts of data for chemical fingerprinting, toxicological profiles, biological and ecological functions in a yet unachieved resolution are emerging [14, 15]. These data offer novel insights to anticipate impacts on biodiversity and ecosystem services as basis for informed decision making. Yet, the full potential of such information can only be realized if it becomes accessible to a larger scientific community and if the digitalization is complemented with tools to derive the new knowledge and options for societal problems. The European Collaborative Projects SOLUTIONS [16], MARS [17], GLOBAQUA [18] and the NORMAN network *(https://www.norman-network.net/)* [19] have demonstrated how European research can provide the platforms for such large-scale data exchange between the scientific community and regulators, taking advantage of increasing digitalization and big data mining, and providing means to transform information into knowledge useful for decision making.

We are facing large-scale environmental challenges that call for transformative thinking and scientific expertise needs to be mobilized to address them adequately. The European Union organized support for excellent international research teams within their Framework Programmes to develop coherence in the European Innovation Union [20]. Such an unprecedented level of integrated European environmental research efforts is seen internationally as a major success story, because it provides scientific evidence and competitive solutions directly in support of European policies and practices on environmental protection and sustainable development. Given the current challenges, these are strong arguments to further support and strengthen European collaborative research, to address the challenges related to (1) the prediction, monitoring, assessment and management of increasingly complex contamination and multiple stressor exposure, (2) minimizing pressure on health, biodiversity and ecosystem services, (3) developing options for smart, sustainable and healthy cities and landscapes, and (4) support sustainable agriculture and industrial innovation and production.

The present paper gives recommendations for strengthening European collaborative applied research to achieve the European environmental policy goals. It has been written on the basis of the experience of the large EU-funded projects SOLUTIONS, MARS and GLOBAQUA. The extensive scientific results of the three projects are documented in about 200 publications each, accessible via the websites *https://www.solutions-project.eu/, http://www.mars-project.eu/, http://www.globaquaproject.eu/en/home/*, and have been exploited to derive a series of policy briefs published in this journal [21–32]. We made no attempts to summarize these results here but drew conclusions for the requirement of future European research under systematic involvement of major stakeholders using a small selection of general achievements of the projects to underline these conclusions.

RECOMMENDATIONS

- *Specify the needs and opportunities for science-based options in support of a non-toxic environment* Contamination of European water resources with mixtures of pesticides, biocides, pharmaceuticals, and other pollutants should be tackled as a complex, multi-dimensional challenge. The additional impact of non-chemical stressors deriving from, e.g., climate change which can alter chemical exposure and effects through water scarcity and thus decreasing dilution of pollution, or the remobilization of contaminants during more frequent flood events have to be seen in concert. Moreover, factors enhancing chemical pressures that have to be accounted for include urbanization and demographic and land use changes inducing rising emissions of pharmaceuticals and personal care products or higher demand for water reuse, respectively. Innovative chemical management in conjunction with sustainable land use and agriculture to counteract the current losses in biodiversity and safeguard ecosystems goods and services requires innovative 'out-of-the-box' thinking. EU research for the Water Framework Directive may prove an example of how collaborative European environmental research can support implementation and advancement of European policies.
- *Establish European collaborative and interdisciplinary research projects* to (i) develop options for comprehensive reduction of modern society's footprints in the nexus of growing demands on energy, food and clean water, (ii) provide the scientific underpinnings for a non-toxic environment, and (iii) protect health, biodiversity and ecosystems goods and services from being jeopardized by exposure to increasingly complex chemical mixtures and non-chemical stressors. Integrated projects should thus aim to:

    - Develop concepts, approaches and methods to close knowledge gaps for chemical mixtures and multiple stressors assessment, e.g., through adverse outcome networks. Emerging and promising methods for a more holistic diagnosis and impact assessment should be advanced including chemical and bioanalytical non-target screening, high-throughput (eco)toxicological profiling, OMICs methods, and human and ecological health monitoring programmes;
    - Survey the 'universe of chemicals' that our societies deal with, currently and in the foreseeable future as a basis for a systematic understanding, and management of exposure to and effects of this chemical universe at different scales;
    - Identify vulnerable species, ecosystems and human populations and prioritize human activities and source regions for abatement. This includes inventories of stress and pollution patterns as well as the development of comprehensive data repositories, computer tools and models to diagnose and predict stress profiles in space and time;
    - Develop long-term strategies for the integrated monitoring, assessment and management of chemical and non-chemical stressors on a European scale and test them in model landscapes in close collaboration between academia and public bodies, industry, agriculture, environmental associations and citizens;
    - Provide a coherent framework for sustainable chemistry comprising chemical invention ('benign by design'), production, distribution, use, waste, fate and effect management across all chemical uses including a dynamic process perspective for progress in knowledge (i.e., accommodate for cross-talk between monitoring and prospective risk assessment);
    - Integrate ecosystem services into environmental management and planning to facilitate a more comprehensive assessment of environmental quality. This provides options to become a driver of societal acceptance and associated policy formulation. In support of this concept, a participatory Ecosystems Services approach for pressure prioritization that enables the integration of Ecosystem Services into River Basin Management Plans would allow a systematic way to prioritize pressures with metrics that directly match with matters that are important for people [33].
    - Develop strategies for urban water and pollution management to support smart, sustainable and healthy cities including the assessment of transboundary chemical footprints [34], advancing on the concept of source-related discharge signatures [35] and fingerprints [14];
    - Foster science–policy interaction for strengthening policy coherence and harmonized cross-compliance of regulations on chemical, water, energy and environmental conservation and to anticipate upcoming transition pathways, e.g., for implementing a circular and bio-based economy.

- *Foster the involvement of non-EU partners in European collaborative research* The realization of the UN SDGs is a global challenge. Mounting environmental deterioration on a global scale will also affect health and welfare of European citizens. For many developing and emerging economies, European regulation and research on chemicals and environmental protection provide valuable options as solutions for environmental problems and thus also assist in keeping anthropogenic impacts within planetary and regional boundaries as a safe operating space for humanity [36]. Common funding instruments and encouraging collaboration with research groups from the United States, Canada, Australia, Japan, China, Brazil as well as developing countries on applied environmental science and pollution research will more efficiently identify major drivers, mobilize additional resources and expertise towards a non-toxic environment and sustainable development on a relevant scale.

- *Complement European research with targeted national scientific funding* to provide incentives for inventions regarding specific scientific questions and to support the evaluation, demonstration and implementation of novel concepts and approaches on a regional scale. The projects SOLUTIONS, MARS and GLOBAQUA may serve as examples, as they developed novel consistent approaches for protection, monitoring, assessment and management of water quality, chemical contamination and multiple stressors. National projects provided follow-up on approaches for regional and national water bodies and river basins in close collaboration with stakeholders from agencies, water supply, wastewater treatment, agriculture, fishing industry and municipalities, NGOs, and others. This collaboration of science and stakeholders on a regional level will provide new opportunities of implementation of protection, monitoring, assessment and management options identified in European research. In addition, specific scientific questions fostering detailed process understanding and specific instrumentation can be addressed efficiently at national levels.
- *Provide incentives for solution-oriented approaches* that allow becoming more creative in chemical innovation and management. We need to depart from the route of one-dimensional thinking of current individual chemical risk assessment and generate more flexibility, e.g., by allowing for weight-of-evidence-based approaches. Collaborative European environmental research is a powerful tool to identify options and alternative trajectories in a world changing to biobased and circular economy approaches. Management action could often be taken before final conclusive statements about a single chemical's hazards and risks are available. Assessing different a priori abatement options for challenging problems rather than producing finite a posteriori status assessments may often be more efficient to derive sustainable solutions [37]. Strategies to develop smart solutions based on sparse data are needed. Emerging transition pathways such as repurposing of waste, which involve fundamental changes in chemical life cycles need incentives.
- *Encourage multi-stakeholder involvement in EU collaborative projects to capture added value and address complexity* Solution-oriented research needs to go beyond the scientific community and needs to engage with the private sectors, governments, citizen groups and environmental organizations [12]. Multiple stakeholder participation in ambitious integrated research projects can play several roles. They function as emphatic safeguards regarding the project's principal objectives. They facilitate the necessary development of overall objectives into operational issues. They foster a science–society dialogue and they help to communicate and translate project findings for non-scientific audiences. Moreover, they are crucial to develop and conduct demonstration projects, pilot and case studies as well as wider acceptance for necessary actions. Crucially, they serve to explore and define a far wider 'solution space' in which innovative transition scenarios can be defined beyond disciplinary boundaries. Stakeholder involvement helps finding solutions for complex problems, as long as the different roles of scientists and stakeholders are acknowledged. Scientists work from scientific facts, while solutions additionally require specific attention to governance issues and transition pathways, which can be anticipated by stakeholders. Thus, for collaborative projects, intensive stakeholder dialogue is often highly beneficial, as long as stakeholder participation is professionally organized from the very beginning of a project. Deciding on options provided by research projects is a policy issue and close interaction with stakeholders significantly enhances the chances of actually implementing the solutions provided by a project in a relevant time frame.

REQUIREMENTS

Investing in EU collaborative projects in the field of research on sustainable use of chemicals, the environment and its services to humanity calls for:

- Recognition that it is required to employ novel concepts and approaches to comprehensively address, assess and manage the 'universe of chemicals' which modern societies rely on for various services and simultaneously reaching the SDGs;
- Acknowledgement that our current rate of innovation and trends in consumption require tools that adequately help to evaluate the likelihood of harm imposed by complex mixtures (both predictive and preventive as well as diagnostic and curative);
- Realization of the needs to be inclusive of human and environmental health, and provide for dynamic changes

in human–environmental interactions, as well as account for the relevance of potential interaction between different stressors in a climate change context;

- Establishment of funding instruments for collaborative projects that explore and develop novel routes of solution-oriented assessment and management to safeguard biodiversity, ecosystem services, and human health;
- Consideration of the specific characteristics of collaborative environmental research that have less focus on marketable products and business development but strives for providing scientific evidence for the achievement of the policy and societal goals of the EU concerning public goods;
- Awareness that understanding, and advanced monitoring, assessment and management of chemical mixtures and non-chemical stressors in European water resources may change our knowledge on causes and sources of risks and thus will support low-footprint cities, sustainable food, industrial and energy production not the least by avoiding costly remediation of contamination;
- Effective demonstration and evaluation in case studies involving stakeholders at different spatial scales and covering regional differences in geographies, land use and cultural context.

ACHIEVEMENTS

APPLIED, COLLABORATIVE, INTERDISCIPLINARY RESEARCH ON A EUROPEAN SCALE

The EU-funded projects SOLUTIONS, MARS, and GLOBAQUA with a total funding volume of over 20 million Euro and comprising 80 leading scientific institutes from 23 European countries together with partners from Australia, Brazil, China, Turkey and Morocco provided the critical mass to successfully overcome the interdisciplinary challenges of monitoring, assessment and protection of European water resources as established in the WFD and the EU strategy for a non-toxic environment. The balance between individual objectives and approaches of the projects and intensive exchange and collaboration between the projects allowed for overarching conclusions directly informing decision making in the catchments and in European regulation. That is, MARS developed an overarching concept to assess how multiple stressors affect surface water and analysed stress data at the European, at the catchment and at the water body scale, providing methods to support improving ecological status in a multiple-stress context. SOLUTIONS contributed a comprehensive picture of contamination and toxic stress in European catchments using predictive modelling based on emission data as well as monitoring of complex mixtures and effects at the watershed scale in major European river basins including those of the Rivers Danube, Rhine and Ebro. GLOBAQUA studied multiple stressor effects in rivers of southern Europe such as the Adige, Evrotas and Sava, providing methods to tailor the aforementioned approaches to water systems under water scarcity scenarios. Together, the projects provided methods to monitor, assess and manage chemical mixtures and other stress that allow for advanced assessment of both chemical safety and ecological status. Collaborative modelling and monitoring data assessments across the three projects revealed that chemical mixtures occur as one of the prevailing factors for determining the ecological status in many rivers. Pollutants collectively contribute in multiple stressor settings to a similar degree as nutrients, hydrology and riparian land use, with a spatiotemporal variability that relates to land use and season. To better understand toxic stress under water scarcity as an increasing challenge under climate change, SOLUTIONS and GLOBAQUA closely collaborated on the Iberian Peninsula and were able to demonstrate the intensifying role of climate change on the environmental impact of chemicals. These results, which emerge from collaborative, interdisciplinary European research, suggest that the separate consideration of chemical contamination (status) and ecological status needs to and can be overcome to achieve the goals of the Water Framework Directive (WFD).

Although strongly focused on fulfilling societal and regulatory demands, applied research, as it has been performed in the three European projects, addresses the full chain of knowledge from basic understanding of scientific processes via monitoring and assessment tools to the formulation of recommendations for protection and management efforts by all stakeholders, supported by a comprehensive set of policies. This may be illustrated by the monitoring of toxic stressors in European water bodies as performed in SOLUTIONS. Starting with the collation and investigation of modes of action and toxicogenomics of known water contaminants [38, 39], an effect-based monitoring strategy and the corresponding toolbox [24] were developed, rigorously evaluated and adapted using selected chemicals [40], mixtures [41] and field samples [42]. Through extensive stakeholder dialogue, policy-related working groups, workshops, via scientific and popular publications plus close collaboration with relevant science–policy interaction networks such as NORMAN, the new concepts were discussed, refined and integrated in the decision-making processes regarding the review of WFD [43].

SOLUTION-BASED APPROACHES IN MONITORING, ASSESSMENT AND MANAGEMENT OF RISKS OF COMPLEX CHEMICAL MIXTURES AND MULTIPLE STRESSORS

While current evaluations of chemical pollution in European surface waters focus on problem description and water quality classification, the projects SOLUTIONS, MARS and GLOBAQUA put emphasis on early exploration of prevention and abatement options considering the remedial space within the Drivers–Pressure–State– Impacts–Response (DPSIR) causal approach [32]. To facilitate solution-focused risk assessment [37], a conceptual framework has been developed [16]. The early consideration of possible responses is supported by a database on technical abatement options [44] and a systematic evaluation of non-technical abatement options. SOLUTIONS-focused assessment of multiple stressors is supported by the SOLUTIONS' Tools and Services for River Basin Toxicants Assessment and Management accessible through the web-based guidance tool RiBa- Tox (*https://solutions.marvin.vito.be/* [29]) and by a living database architecture for the exchange of chemical and effect-based monitoring data [30]. Moreover, a scenario analysis tool developed by MARS provides indications on how stressor intensity and ecological status will develop under given scenarios of human impact at the European scale and broken down to more than 100,000 sub-catchments in Europe *(https://mars-project-sat.shinyapps.io/mars-sat)*. In addition, a diagnostic tool developed by MARS assists water managers to identify the main stressors affecting the ecological status, and to derive appropriate management measures *(http://freshwaterplatform.eu/index.php/mars-diagnostic-tools.html)*. GLOBAQUA developed ESPRES (Efficient Strategies for anthropogenic Pressure Reduction in European waterSheds, *http://www.globa qua-project.eu/en/content/ESPRES-tool.94*/), a web-based decision support tool that can be employed to explore management options for achieving environmental targets of European water bodies. The user-friendly web interface supports multicriteria river basin analyses via DPSIR-based causal analysis steps to identify efficient pressure reduction strategies and reflecting the perception of stakeholder efforts, which includes monetary costs, political difficulty, and social acceptability of available solutions. Monitoring and assessment of ecosystem goods and services such as river ecosystem functioning have been addressed by GLOBAQUA and recommended as a crucial module to be included in the existing river monitoring and assessment schemes [45]. The resultant toolbox is accessible *(http://www.globa qua-project.eu/en/content/Toolbox-for-ecosystem-functioning.50/)*.

SUCCESS MEASURES TOWARDS A NON-TOXIC ENVIRONMENT AND SUSTAINABLE CITIES AND LANDSCAPES

While global boundaries have been defined as the safe operating space for humanity [36], ecological, energy, carbon and water footprints have been introduced to quantify the appropriation of natural resources by humans within these boundaries [46, 47], typically at a regional scale. Chemical footprints as applied in SOLUTIONS were likewise developed as an indicator of the cumulative impacts of chemical mixtures on biodiversity and represent the approximation or exceedance of a contamination level considered as safe [48]. They are recommended to be used to evaluate trends in chemical contamination and may help selecting best options for abatement scenarios, as well as to communicate complex data sets on mixture exposures and effects [32]. To anticipate the effectiveness of interventions, the perspectives of the water cycle and the chemical life cycle were connected by providing a mitigation database coupled to hydrological models [44].
River basin scale case studies were instrumental to benchmark performance of modelling and measurement tools for water contamination assessment, provided data necessary to identify river basin-specific pollutants, demonstrated the benefits of the technical upgrade of wastewater treatment plants, specified the potential for targeted remediation of pollution sources, and demonstrated the interactions between contamination and situations of water scarcity that need to be acknowledged. In particular, we sought to conceptually provide links for bridging between chemical and ecological water status measures [49–51]. This includes the identification and ranking of environmental hazards with ecosystem vulnerability distributions [52]. Thus, we overcame a major hurdle in current water quality assessment, where ecological and ecotoxicological assessments and recommendations are derived independently, based on different principles (protection vis a vis protection and impacts) leading to diverging, if not contradictory advice for river basin management.

SCIENCE–POLICY INTERACTION AND STAKEHOLDER DIALOGUE

Starting in the proposal phase, a systematic and structured dialogue with diverse stakeholders was established in the three collaborative projects SOLUTIONS, MARS and GLOBAQUA. It involved major stakeholders in the fields such as DG Environment, European Environmental Agency (EEA), European Chemical Agency (ECHA), European Food Safety Authority (EFSA), International River Commissions such as International Commission for the Protection of the Danube River (ICPDR) and the Rhine (ICPR), national environmental and chemical agencies, water industry, and NGOs. The structured stakeholder dialogue led to joint activities and developed new options. For example, SOLUTIONS provided the compilation of river basin-specific pollutants suggested for the Danube River Basin Management Plan and provided conceptual and technical input as well as case study evidence to the sub-group for effect-based methods of the CIS Working Group Chemicals under DG Environment. MARS with stakeholder participation developed conceptual models on how the relevant multiple stressors affect water body status in sixteen case study catchments and subsequently used the outcome for producing predictive models. The results were discussed in a specific workshop with the Common Implementation Strategy (CIS) Working Group ECOSTAT of DG Environment.

A moderated e-learning course for policy makers and river basin managers was provided to translate scientific understanding for end users *(http://www.globaqua-project.eu/en/content/E-Learning.93/)*.
In summary, the three projects SOLUTIONS, MARS and GLOBAQUA provided well-structured and complementary contributions to the EU policy goals on sustainable management of water resources. Acknowledging a growing world population with growing demands for agricultural, industrial and energy production under conditions of climate change, land use changes and urbanization pressures and management needs emerge at a novel scale. We need to jointly address toxic pressure by complex mixtures of chemicals and multiple stressors from various sources across compartmental and regulatory borders and enable their prediction, monitoring, assessment and abatement. Accounting for associations and nexus between SDGs is a major challenge for which scientific as well as practical solutions are sought that circumvents undue trade-offs between SDGs. The water quality-related projects GlobAqua, MARS and SOLUTIONS may serve as examples for the performance of collaborative projects in supporting a rational European policy on sustainability, environmental protection, and for safeguarding of ecosystem services for "living well, within the limits of our planet" [13].

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this paper at *https://doi.org/10.1186/s12302-019-0232-y*.

Abbreviations

CIS: Common Implementation Strategy; DG: Directorate General; DPSIR: Drivers– Pressure–State–Impacts–Response; ECHA: European Chemical Agency; EEA: European Environmental Agency; EFSA: European Food Safety Authority; EU: European Union; ICPDR: International Commission for the Protection of the Danube River; ICPR: International Commission for the Protection of the Rhine; NGO: Non-Governmental Organisation; SDG: sustainable development goals; UN: United Nations; WFD: Water Framework Directive.

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POLICY BRIEF

solutions

EFFECT-BASED METHODS ARE KEY. THE EUROPEAN COLLABORATIVE PROJECT SOLUTIONS RECOMMENDS INTEGRATING EFFECT-BASED METHODS FOR DIAGNOSIS AND MONITORING OF WATER QUALITY

ABSTRACT

The present monitoring and assessment of the chemical status of water bodies fail to characterize the likelihood that complex mixtures of chemicals affect water quality. The European Collaborative Project SOLUTIONS suggests that this likelihood can be estimated with effect-based methods (EBMs) complemented by chemical screening and/or impact modeling. These methods should be used to identify the causes of impacted water quality and to develop programs of measures to improve water quality. Along this line of reasoning, effect-based methods are recommended for Water Framework Directive (WFD) monitoring to cover the major modes of action in the universe of environmentally relevant chemicals so as to evaluate improvements of water quality upon implementing the measures. To this end, a minimum battery of bioassays has been recommended including short-term toxicity to algae, Daphnia and fish embryos complemented with in vitro and short-term in vivo tests on mode-of-action specific effects as proxies for long-term toxicity. The likelihood of adverse impacts can be established with effect-based trigger values, which differentiate good from poor water quality in close alignment with Environmental Quality Standards for individual chemicals, while taking into account mixture toxicity. The use of EBMs is suggested in the WFD as one avenue to establish the likelihood of adverse effects due to chemical pollution in European water systems. The present paper has been written as one component of a series of policy briefs to support decisions on water quality monitoring and management under the WFD.

CHALLENGE

In line with the EU strategy for a non-toxic environment [1], the Organisation for Economic Co-operation and Development (OECD) Council Recommendation on Water [2] and the Sustainable Development Goals by the United Nations [3], protecting water resources from contamination with toxic substances is a major task of water quality assessment and management. Water quality assessment according to the European Water Framework Directive [4] is presently based on chemical analysis of 45 Priority Substances (PS) [5] to assess the chemical status together with different sets of River Basin-Specific Pollutants (RBSP) defined nationally, currently a total of approx. 300 in the different EU member states. It has been demonstrated that these substances reflect only a (site-specific and typically unknown) fraction of the overall chemical risk [6] and mixture risks are not considered. Thus, the current approach is insufficient to estimate the likelihood that chemical contamination causes harm to human health or aquatic ecosystems, and to develop programs of measures to reduce chemical pollution impacts. In the WFD, chemical pollution is defined as any chemical or mixture that poses harm (Article 2).

European surface waters contain tens to hundreds of thousands of chemicals including pesticides, biocides, pharmaceuticals, surfactants, personal care products and many more together with numerous transformation products. These chemical cocktails may pose a risk to ecosystems and raise concerns for human health if water resources are used for drinking water production, fishing and recreation. The focus on PSs and RBSPs encourages reduction in their use, but replacement of these substances by alternatives that pose similar hazards is an unresolved problem. Chemical monitoring of a few selected individual chemicals is and will increasingly be less informative for identifying the likelihood that chemical mixtures pose harm, whilst the probability of overlooking significant risks is high and increasing. As a result of the application of management measures, prioritized chemicals tend to be replaced by non-prioritized (non-regulated) ones that have often similar effects. This process increases the relative contribution of non-prioritized chemicals to the overall risk. A strategy that would focus on monitoring the concentrations of all chemicals on the market would practically fail. The logical solution for taking into account missing, and potentially harmful, chemicals would be to use integrative methods to evaluate the likelihood of complex mixtures causing harm.

Thus, the challenge is to characterize chemical pollution in a comprehensive way with limited resources, such that the impact of chemical pollution can be diagnosed, that risks to ecosystems and human health can be prevented, that resources for safe drinking water production can be protected with limited treatment costs, and that improvements through programs of measures can be monitored.

RECOMMENDATIONS

- Implement effect-based methods (EBM) techniques to improve the “Analysis of Impacts” (diagnosis) under WFD-Annex II to (a) support water management with adequate information on the risks posed by the ‘universe of chemicals’ [7], and (b) enable monitoring of the success of programs of measures in improving water quality. EBMs are bioanalytical methods using the response of whole organisms (in vivo) or cellular bioassays (in vitro) to detect and quantify the effects of groups of chemicals on toxicological endpoints of concern. EBMs are helpful

    – For detecting the effects of mixtures of compounds in water resources and demonstrating their potential to affect aquatic organisms and human health,
    – For minimizing the risk of overlooking hazardous chemicals, transformation products and chemical mixtures,
    – For detecting hot spots of contamination for investigative monitoring,
    – For identifying risk drivers and prioritizing them for management measures,
    – For linking chemical and ecological status.

- Use the guidance on available EBMs to integrate the EBMs into a solution-oriented water quality assessment and monitoring strategy to support River Basin Management Planning
- Use a battery of bioassays covering major (eco) toxicological endpoints, which can be achieved by employing

    – Apical bioassays representing at least fish (96 h fish embryo acute toxicity), invertebrates (48 h daphnia immobilization) and algae (72 h inhibition of population growth) considered as Biological Quality Elements (BQE) for pelagic communities under the WFD and
    – In vitro assays addressing specific modes of action (MoA), such as specific assays addressing endocrine disruption, mutagenicity and activation of cellular defense mechanisms.

- Apply sample enrichment before applying EBMs to separate organic micropollutants from other matrix components and to increase sensitivity of EBMs so that robust data based on concentration-effect models are derived and detection limits for hazardous chemicals equivalent to Environmental Quality Standards (EQS) of PS and RBSP are achieved.

- Adopt regulatory frameworks supporting EBM application for diagnosing whether or not complex mixtures are impacting water quality and for monitoring in a way that not only addresses currently established effects but also allows for tackling endpoints of emerging concern. This is necessary since it may be expected that opening monitoring for EBMs will trigger the development of new cost-efficient methods that will address MoAs that are not yet covered.
- Use EBMs for identifying the need for abatement measures and assessing their efficiency. If EBMs indicate unacceptable risks, decisions on measures can be taken without knowing the individual drivers of the risk. Examples are the observation of enhanced toxicity downstream of the discharge of effluents that may be abated with improved treatment technologies using advanced oxidation processes or activated carbon or toxicity abatement downstream of agricultural areas by applying extended buffer strips along the stream. The comparative application of EBMs upstream and downstream the discharge indicates the success of the measure in a cost-efficient way without the identification of individual chemicals. Moreover, the WFD suggests combining Lines of Evidence, whereby EBM results can be combined with other approaches such as emission inventories, pollutant concentration measurements and ecological monitoring data.
- Use effect-directed analysis (EDA) if EBMs indicate unacceptable risks that are expected to be driven by site-specific chemicals for example from industrial processes that should be better avoided or treated at the source rather than with end-of-pipe treatment. A comprehensive overview on available EDA tools is available [8].
- Combine EBMs with chemical analytical screening at priority sites for the identification of important risk drivers at a larger scale, contamination trends, newly emerging chemicals and spills to prioritize chemicals for regulation and as integrated early warning tools for upcoming pollution problems.

REQUIREMENTS

Integrating EBMs into both diagnosis (Annex II) and/or surveillance, operational and investigative monitoring for water quality management requires:

- Recognition that—given current concerns on water quality and adverse trends as well as the WFD definition of 'pollution' related to *all* chemicals—it is required to employ methods that enable the evaluation of the hazards of the whole 'universe of chemicals' where needed;
- Recognition that effect-based monitoring is one of the operationalized methods providing information along one of the lines of evidence mentioned in the WFD (Annex II) to evaluate the likelihood of harm of complex mixtures (diagnosis);
- Agreement on and the establishment of a coherent battery of bioassays in order to cover modes of actions of all chemical groups considered to potentially pose harm to ecosystems and human health. This is supported by the experience and expertise in SOLUTIONS and the NORMAN network on emerging substances;
- (Further) standardization of EBM-test systems with a focus on robust, small-volume and high-throughput assays to facilitate practices;
- Agreement on and use of effect-based trigger values to assist in interpretation of effect-based monitoring for all EBMs in relation to the need to characterize the likelihood of posing harm;
- Acknowledging and expanding the demonstration and evaluation of EBMs in practice-oriented case studies;
- The design of a roadmap to support the consistent and useful implementation, and interpretation of EBMs for the purposes of the WFD, covering both the use of EBMs to diagnose the impacts of complex mixtures on current water quality as well as to improve surveillance, operational and investigative monitoring of complex mixtures in European water bodies.

ACHIEVEMENTS

COMPILATION OF A BATTERY OF BIOASSAYS

A wide range of EBMs has been applied successfully for both diagnostic and monitoring purposes to assess the likelihood of impacts of chemical pollution, most of them in a scientific development context for establishing robust and meaningful EBM-tools. These activities provided substantial progress towards the compilation of a useful battery of bioassays. First, a comprehensive analysis of about 1000 typical water contaminants identified 31 major MoA categories while for a substantial fraction (37 %) of the compounds no information on MoAs was available [9]. Second, MoA-specific in vitro assays fit for the purpose of environmental diagnosis and monitoring are available for receptor-mediated endocrine effects, genotoxicity and mutagenicity, activation of metabolism, adaptive stress responses, photosynthesis inhibition and cell line-specific cytotoxic effects [10–12]. Thus, in vitro assays address well-described MoAs with known environmental relevance as proxies for long-term effects, although not all potentially relevant effects are covered with present test systems. To also cover chemicals with unknown and non-specific MoAs as well as with MoAs that cannot be addressed with existing MoA-specific in vitro assays and to detect specific impacts on the WFD-Biological Quality Elements, it is recommended to complement these assays with apical short-term toxicity bioassays representing at least fish (fish embryo toxicity), invertebrates (immobilization of daphnia) and algae (inhibition of cell multiplication), which represent BQEs for pelagic communities in WFD (Fig. 1). Amongst the MoA-specific in vitro assays, priority of application should be given to endocrine disruption and mutagenicity. Dioxin-like effects should be analyzed particularly in sediments [13], biota [14] and equilibrium passive samplers [15], since typical drivers of these effects are very hydrophobic and accumulate in these matrices.

STANDARDIZATION AND UTILITY OF TEST SYSTEMS

In SOLUTIONS and the NORMAN network, we proposed a test battery of and in vivo bioassays and published standard operating procedures [12, 16]. The utility of EBMs is found in both the diagnosis and assessment of impacts on ecological status (cf. WFD Annex II) and the monitoring water quality status and trends (WFD Annex V).

AVAILABILITY OF ROBUST ENRICHMENT TOOLS

Solid-phase extraction (SPE) was found to be a suitable sample preparation method for environmental water samples that are to be tested in the aforementioned bioassays, with effect recovery by current SPE methods similar to recovery of individual chemicals by chemical analysis [17]. While sample enrichment is always restricted to an application domain with respect to the physicochemical properties of the chemicals, the “effect recovery” experiments indicated that for the typically applied co-polymer sorbents this domain is sufficiently broad to extract a large share of the overall toxicity of organic chemicals in water [17]. Metals and other inorganic chemicals are not addressed and need to be monitored separately. A robust mobile large-volume SPE has been developed for the use in the field, which avoids the transportation of large water volumes to the laboratory for enrichment [18] and allows for time-integrated as well as event-based sampling. Equilibrium passive sampling may be useful to concentrate hydrophobic chemicals in a biomimetic manner for subsequent EBM application [15]. For screening purposes, samplers for more hydrophilic compounds can also be used [15, 19].

DEMONSTRATION AND EVALUATION IN CASE STUDIES

In SOLUTIONS, EBMs were applied in a series of case studies, where it was possible to characterize the likelihood that complex mixtures present in water systems pose specific (MoA-related) harm to the Biological Quality Elements, along a river stretch [20], around wastewater treatment plants [21, 22] and close to inflows of untreated wastewater [23]. For the selected types of example sites, mutagenic, estrogenic, androgenic and anti-androgenic effects could be established as markers for the likelihood that treated and untreated wastewater affects aquatic life. In addition, the methods allowed the impact of wastewater effluents on surface water quality to be estimated and the overall effects of chemical pollution on aquatic life and thus water quality to be assessed. The methods helped identify damage and associated causes (diagnosis, Annex II) in support of water quality management. Examples are the detection of strong antiandrogenic effects in the River Holtemme (Germany) and the identification of the fluorescence dye coumarin 47 as the cause of this effect [24], the detection of mutagenicity in the Rivers Mulde and Rhine and the identification of diaminophenazines [22] and synergistic effects of aromatic amines with natural alkaloids [25] as mutagenicity drivers. These examples may also underline how monitoring (Annex V) with EBM’s can help evaluate status and trends.

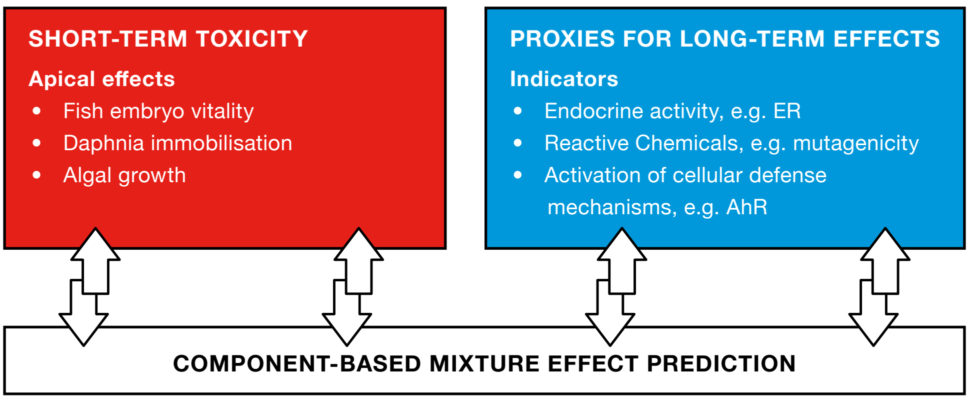

Fig. 1: Recommended test battery of in vivo (red) and in vitro (blue) bioassays. *ER* estrogen receptor, *AhR* aryl hydrocarbon receptor

Quality/performance criteria for the benchmarking of estrogenicity bioassays have been recently investigated in an inter-laboratory comparison study [26]. In a Europe-wide demonstration program supported by SOLUTIONS, the NORMAN network, the Swiss Centre for Applied Ecotoxicology and the Joint Research Centre of the European Commission, the reliability of EBMs for screening of estrogenic compounds was analyzed to harmonize monitoring and data interpretation methods, and to contribute to the current WFD review process. Surface water and wastewater samples were collected across Europe and analyzed using chemical analyses and EBMs. The study demonstrated that the inclusion of effect-based screening methods into monitoring programs for estrogens in surface waterbodies is a valuable complement to chemical analysis because of the lower LODs of the EBMs in comparison to chemical analysis [27, 28]. Based on the results and achievements of SOLUTIONS and the NORMAN network, such comprehensive case studies should also be performed for other modes of action.

DEVELOPMENT OF EFFECT-BASED TRIGGER VALUES (EBT)

Effect-based trigger values (EBT) have been developed for many EBMs. EBTs are expressed as bioanalytical equivalent concentrations (BEQ) and can be read across from existing EQS values for single chemicals. EBTs basically define an acceptable level of effect (translated into EBT-BEQ), in close alignment with the WFD protection goals and concentration-based Environmental Quality Standards (EQS), which proved to be useful for interpreting EBM-results in relation to the likelihood to pose harm [28, 29]. Bioassay-specific EBTs were derived by translating individual annual average (AA)-EQS for single dominant chemicals such as estrogens into EBT-BEQs [26, 28, 29], by ecological considerations and application of species sensitivity distributions [30] or by reading across from all existing EQSs using a transparent algorithm that does not require any user assumptions or judgements about the data [29]. The latter EBT-derivation method targets undefined mixtures acting according to a specific MoA. In contrast to EQSs, EBTs consider all chemicals in a mixture contributing to measured effect. Thus, this approach does not require individual guideline values for all mixture components of a mixture. Bioassay-specific EBTs are key for the interpretation of results from water quality assessment, as effects below the corresponding EBT indicate a low likelihood that the chemical mixtures pose harm whilst exceedance implies increasingly clear indications for harm to aquatic life. Importantly, the proposed approach can be applied to any bioassay provided there are sufficient effect data available.

SUPPLEMENTARY INFORMATION

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