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Use cases from the German NTSPortal on the systematic use of high-resolution mass spectrometry non-target screening data in environmental monitoring and chemicals management

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Abstract

Background Society aims for a pollutant-free environment, reflected in initiatives under the European Green Deal, which seek to reduce hazardous substances and promote safe, sustainable chemical use. Comprehensive exposure data are needed to identify sources, understand mixtures and eliminate sources of chemical pollution. High-resolution mass spectrometry non-target screening (HRMS NTS) is increasingly used in environmental regulatory context to chemically characterise the environment as completely as possible and retrospectively screen for known and emerging substances.

Results This study provides use cases for monitoring and chemicals management with data from the German NTSPortal, a database and visualisation tool for HRMS NTS data from surface water and suspended particulate matter of major German rivers. Its internal spectral library enables substance identification comparable to standardised target analysis, supporting regulatory acceptance of HRMS NTS data for prioritisation and mixture assessment. To demonstrate its potential to research and regulation, we characterised the spatial and temporal distribution of riverine chemical mixtures and present selected use cases relevant to EU environmental, emission, and chemical legislation. Despite pronounced spatial variability, mixture composition based on presence–absence data remained stable over time, with 855 of 1721 substances detected at least once and 247 occurring ubiquitously. Declining trends for regulated substances such as carbendazim and climbazole illustrate the effectiveness of regulatory measures. Overall, the results showed that NTS data repositories can help overcome fragmented exposure information and enable more consistent use of monitoring data across policy areas, including evaluation of the revised Urban Waste Water Treatment Directive and One Health concepts.

Conclusions Data from the German NTSPortal enabled a multi-matrix and temporal characterisation of riverine chemical mixtures, revealing both stable mixture compositions over time and persistent, catchment-specific substances. These data facilitated high-resolution mixture assessments across space and time, alongside trend analyses that meet regulatory needs in environmental monitoring and chemical risk assessment. Further temporal, spatial, chemical and matrix-spanning expansion of HRMS NTS repositories will enhance their value for environmental monitoring programmes. Strengthening interoperability, implementing FAIR data principles, and developing advanced tools for prioritisation, quantification and toxicity prediction, including AI-based approaches, will be crucial to fully realise the regulatory potential of NTS portals in the future.

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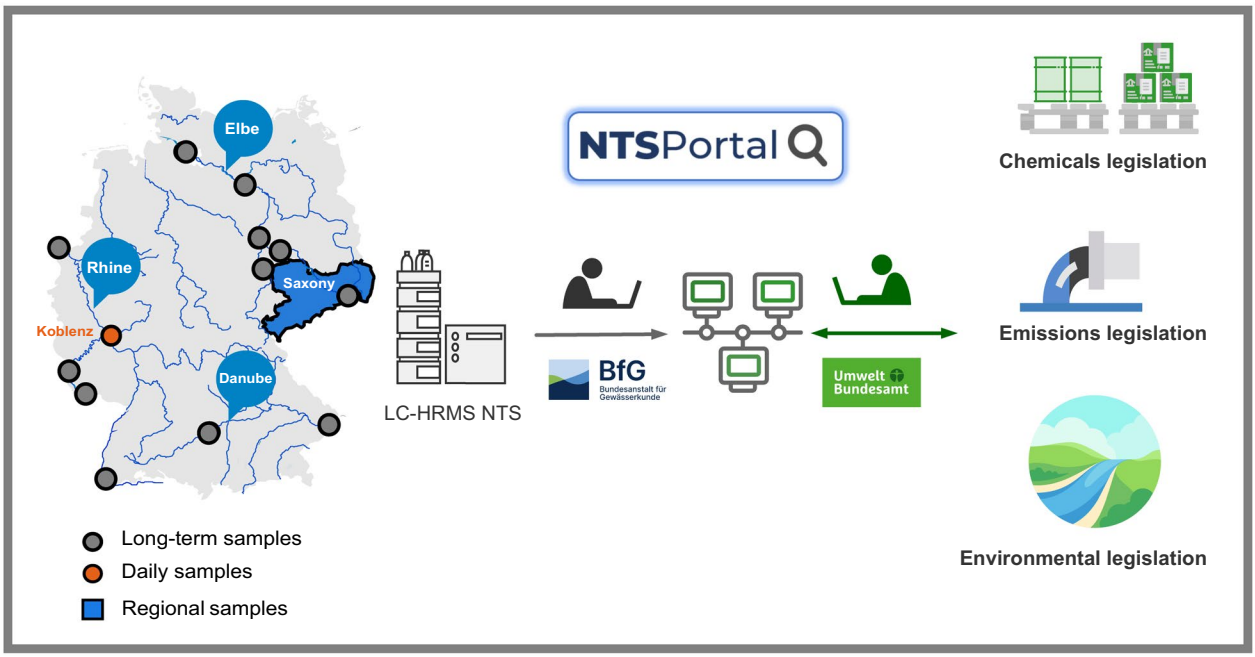
Keywords HRMS, Non-target Screening, Monitoring, Chemicals management, Environmental policy, Risk assessment, Water Framework Directive, REACH, Suspended particulate matter

Graphical abstract



Background

Society aims for a pollutant-free environment, as reflected in the European Green Deal, the EU Zero Pollution Action Plan and the EU Chemicals Strategy for Sustainability, which promote a toxic-free environment and safer, more sustainable chemical use [1–3]. These initiatives respond to the need for better knowledge on chemical exposure to identify sources, understand mixture effects and eliminate the causes of chemical pollution [4, 5]. To overcome present gaps between monitoring and risk assessment for marketed substances in the EU, the emerging One Substance, One Assessment (OSOA) initiative seeks to *inter alia* improve the shared knowledge base on chemical risks and exposure and strengthen early-warning systems for contaminants of emerging concern [2, 6]. So far, chemical monitoring under EU legislation, notably the Water Framework Directive (WFD), has relied on target-oriented identification and quantification of predefined priority substances to ensure harmonised reporting and basin-wide status assessment across EU Member States [7, 8]. This approach still reflects the analytical capabilities and resources of the early 2000s and uses standardised methods with quality requirements (detection limits, accuracy, precision, reproducibility) to create uniform conditions in regulatory environmental analysis and enable consistent data reporting and status assessment [7]. Over the past two decades, high-resolution mass spectrometry non-target screening (HRMS NTS) has emerged as an innovative approach to characterise environmental mixtures beyond prioritised target lists, which are constrained by prerequisite knowledge and prioritisation [9–12], and to identify unknown, unregulated substances [13, 14]. As in target analysis, detectability hinges on sensitivity, matrix, extraction, and ionisation efficiency, which vary across sample types, instruments and analytes [15–17]. Most of the HRMS NTS data obtained so far originate from liquid chromatography (LC) HRMS measurements. This approach is particularly suited for the detection of moderately polar to polar substances, while substances with very low or very high polarity, as well as volatile substances, are comparatively less accessible and therefore underrepresented in LC-HRMS-based studies [10]. Experience is strongest for waste water and river water; fewer data exist for suspended particulate matter, sediments, and biota from aquatic environments [16, 18].

To realise NTS potential, key challenges include handling large data volumes, reliable feature alignment and componentisation, unambiguous identification, semi-/quantification, and inter-laboratory comparability across matrices [10, 19–21]. Standardisation drives acceptance for regulatory monitoring and risk assessment, building on shared protocols, internal standard mixes, and community platforms [10, 20, 22, 23]. A widely adopted identification framework links confidence to evidence types (MS2 spectra, isotope patterns, reference standards), improving result communication among researchers and authorities [24]. Recent efforts established harmonised aquatic NTS workflows via the European network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances (NORMAN network) [14] and the European Partnership for Assessment of Risks from Chemicals (PARC) [25], complemented by national initiatives from German Chemical Society (GDCh) [26] section Water Chemistry, German Institute for Standardisation (DIN) [27], and Royal Netherlands Standardization Institute (NEN) [28]. These advances have catalysed policy and regulatory interest in leveraging HRMS NTS for chemicals, emissions, and environmental legislation [25, 29–35]. It also led to considerations regarding a digital infrastructure to store, evaluate, and visualise NTS data with three goals: support new laboratory activities, enable joint evaluations across programmes, and preserve datasets for retrospective analysis [21, 36, 37]. Retrospective HRMS screening has been demonstrated for e.g. PFAS, azole-fungicides, and pyrrolizidine alkaloids in different matrices [38–42] with early experience consolidated in NORMAN's Digital Sample Freezing Platform (DSFP) [43, 44].

Germany is establishing a permanent repository (NTSPortal) at the Federal Institute of Hydrology (BfG) for LC-HRMS NTS riverine data from national and state labs, together with the German Environment Agency (UBA), enabling analysis of past, current, and future samples [45, 46]. A comparable infrastructure is currently developed for Swiss cantonal monitoring agencies by Eawag (NTSuisse) for processing and analysis of surface water data for participating cantons and the federal government [47]. In addition, the International Commission for the Protection of the Rhine (ICPR) coordinates the Rhine NTS tool under EU LIFE [48], while several countries are planning or piloting national portals [49–53].

The German NTSPortal uses a conservative screening strategy with an in-house spectral library of several hundred substances characterised by accurately measured m/z values, MS2 spectra and retention times, enabling highly reliable and reproducible feature identification in environmental samples [45, 54]. Although this narrows the exploratory scope of NTS approaches, particularly ignoring the NTS potential to detect unknown substances, in-house spectral libraries enhance instrument- and matrix-specific accuracy, and reduce false positives/negatives compared with generic suspect screening [24, 55, 56]. Their integration into quality assurance/quality control workflows strengthens regulatory acceptance in monitoring and chemical management, and supports semi-quantification and retrospective time-series analysis of HRMS NTS data [21, 26, 41, 57, 58]. In the future, the integration of HRMS NTS workflows to detect unknown substances will increase substance coverage within the NTSPortal and facilitate the use of NTS for early warning systems.

A key asset for the NTSPortal is archived samples from the German Environmental Specimen Bank (ESB) and their HRMS NTS data, which enable retrospective trend analysis over two decades and provide insights into the long-term dynamics of individual substances and complex mixtures.

This study explores the potential of the German NTSPortal for regulatory applications through selected use cases, illustrating how non-target screening-based exposure data can inform chemical management. Although the platform currently supports presence-absence evaluations and intra-substance peak area assessments without integrating effect data, the examined use cases demonstrate its applicability within regulatory workflows. These include developing mixture overviews, addressing specific use categories, and supporting substance-oriented analyses across environmental, emission, and chemicals legislation. We hypothesise that NTS data repositories can play an important role in overcoming fragmented and incomplete exposure information, enabling better access to monitoring data, and achieving more consistent use of exposure information across regulatory and policy areas.

Methods

EU market list

A comprehensive assessment of substances approved or registered for the EU market was carried out to create a curated list of substances and their chemical identifiers, which were linked to the legislation under which they were placed on the market. This list was used to combine data on environmental exposure with the substances' legislation in order to determine which legislation contributes most to exposure.

The Regulation European Commission (EC) 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) [59] is the main EU law to protect human health and the environment from

the risks that can be posed by chemical substances. Under REACH, substances manufactured or imported at ≥ 1 t/a must be registered before they can be placed on the market. Active substances used exclusively in Biocidal Products are not in the scope of the environmental risk assessment in REACH but subject to the Biocidal Products Regulation (EU 528/2012) [60], while co-formulants remain fully subject to REACH obligations. Similarly, chemicals used exclusively as Plant Protection Products (PPP) are authorised under their own regulation [61] (EC 1107/2009), while co-formulants are potentially subject to the full REACH requirements.

In addition, substances used exclusively in Human Medicinal Products (HMP) under Directive 2001/83/EC [62] and Veterinary Medicinal Products (VMP) under Regulation EU 2019/6 [63] have comprehensive exemptions from REACH. Furthermore, other substances were assigned to certain uses that fall under specialised legislations overlapping with REACH, including Cosmetics (EC 1223/2009) [64] and Food Contact Materials (EC 1935/2004) [65], or which are fully exempt from REACH, i.e. additives used in food and feed (EC 1333/2008, EU 872/2012, EC 1831/2003) [66–68].

Substance data were collected from EU agencies, national competent authorities and their networks, harmonised and cleared from duplicates. For each substance, various chemical identifiers and other parameters, such as IUPAC name and InChIKey, were searched for and, where possible, added using CompTox [69], PubChem [70], NORMAN SusDat [71] and the CAS Common Chemistry database [72]. Results from the various databases were compared and the best identifiers and parameters were selected based on the greatest possible consistency of the results. The data, code, and resulting dataset regarding the EU market list will be published in a separate manuscript. Further information is given in Additional File 1.

HRMS NTSPortal

The NTSPortal is a NoSQL ElasticSearch database as well as a web-based application with a graphical user interface using Kibana for annotated HRMS NTS data. Interested users have to set up a user account by provision of a valid e-mail and IP address to ntsportal@bafg.de. Afterwards, it can be accessed at https://ntsportal.bafg.de. Processed HRMS NTS data (internal standard-normalised and absolute peak areas) are saved as individual JavaScript Object Notation (JSON) documents, which are stored in ElasticSearch indices. The individual indices can be downloaded via an Application Programming Interface (API), accessible via R and python, for further analyses. The graphical user interface allows for spatio-temporal data analysis and visualisation in different dashboards. The HRMS NTS data in the NTSPortal has an open license (CC BY 4.0).

Samples and sample preparation

Surface water and suspended particulate matter (SPM) samples from German rivers are currently used for the NTSPortal. Annual composite SPM samples come from the German ESB from 13 sites (Fig. 1) along federal waterways from 2005 onwards (224 samples in total). Sampling and processing were performed according to a standardised operation protocol by [73]. Briefly, the samples were collected monthly from sedimentation boxes (30 L) over the entire years, sieved (< 2 mm), frozen on site above liquid nitrogen, freeze-dried, pooled to annual samples and fractionated to 10 g sub-samples. The ESB provides cryogenic conditions in the archive with temperatures of below − 130 °C, which is below the glass transition temperature of water. Furthermore, samples are stored above liquid nitrogen in an inert-gas atmosphere preventing oxidation processes. This ensures that chemical processes in the samples are reduced to a minimum [73].

Water samples consist of (1) cooled (4–6 °C) daily 24-h composite samples of surface water from a long-term measurement programme at the Rhine measuring station in Koblenz since 2017 (a total of 2924 samples) and (2) surface water samples from a 3-year research project (2021–2023, 530 samples in total) taken from 101 rivers and water bodies of varying sizes in Saxony by the Saxon State Office for Environment, Agriculture and Geology [74] (see Additional File 1). For sample preparation, the SPM samples were extracted with Methanol/ultra-pure water (1:1, v/v, LiChrosolv hypergrade, Merck (Darmstadt, Germany)) according to [75] and the water samples were filtered over 0.45 µm (CHROMAFIL, cellulose acetate) [76].

HRMS NTS measurements, collective spectral library and quality control

Surface water and SPM samples were measured by the BfG using a standardised method [76]. Briefly, 990 µl of prepared samples were spiked with an internal standard (including bezafibrate-d4) to 1000 µl and then measured with an LC/ESI-Quadrupol Time-of-Flight (QTOF) (Agilent 1260 LC with C18 Zorbax Eclipse Plus column and security guard coupled to Sciex TripleTOF 6600) in full-scan MS1 and data-dependent MS2 acquisition mode. SPM samples were prepared and measured in triplicate. Data processing of LC-QTOF raw data was performed according to [46] using the publicly available R package "ntsworkflow" [54].

Processed HRMS NTS data were annotated at Schymanski level 1 [24] via an in-house collective spectral

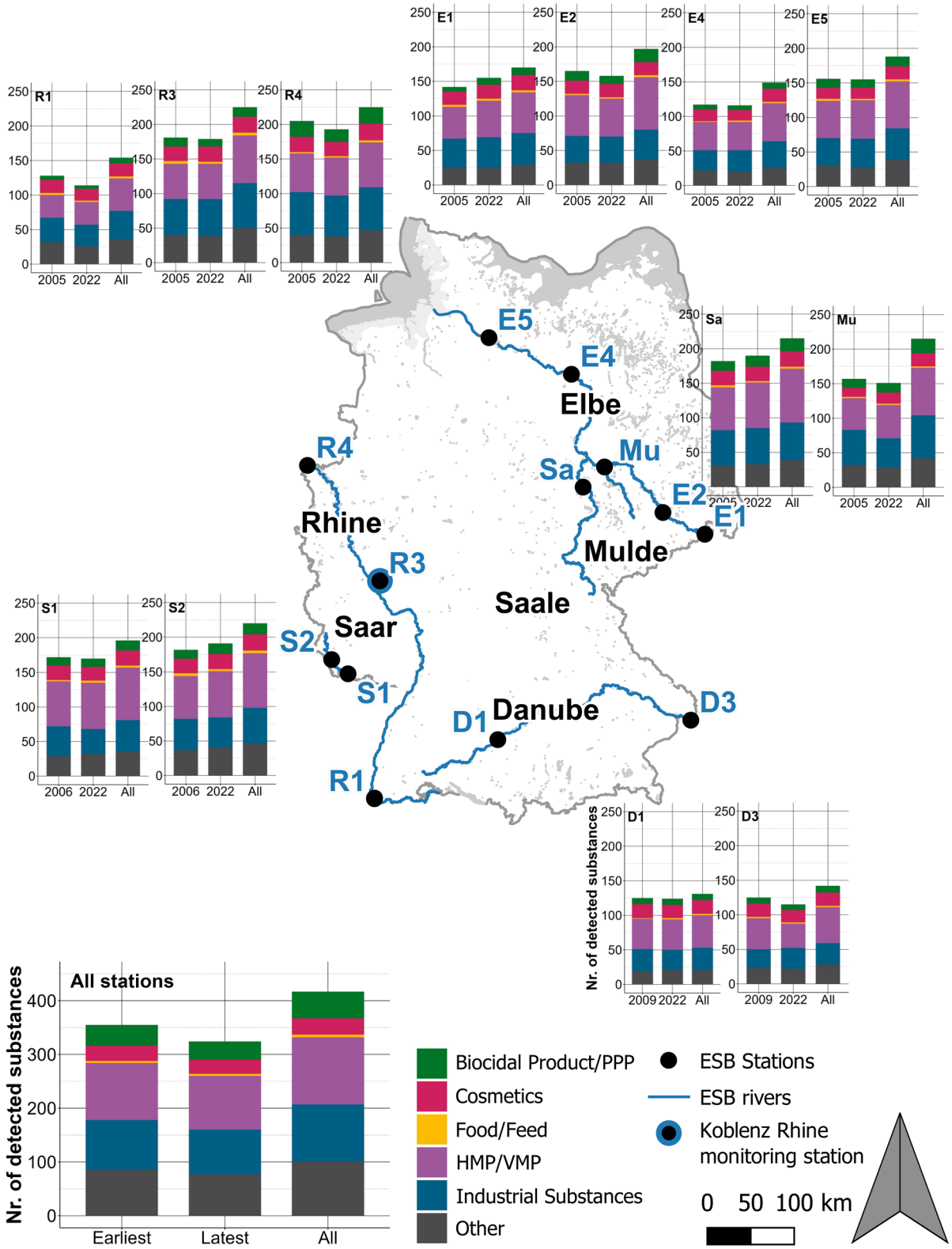


Fig. 1 Map of Germany showing water bodies (grey), rivers analysed in this study (blue lines), Environmental Specimen Bank sampling sites (black points) for suspended particulate matter (SPM), and the Koblenz SPM and water sampling station (black point with blue outline). Bar charts depict the legislation distribution of detected substances at the earliest (left), latest (middle), and across the entire sampling period (right) per site and across all sites (note different y-axis scaling) in SPM samples. Legislation distributions are shown as absolute counts

library (CSL v25.5) containing MS2, retention time and m/z information from 1721 unique substances, which is continuously expanded and made publicly available at MassBank Europe [77]. Four different German laboratories contributed to the CSL: BfG, UBA, Bavarian State Office for the Environment (LfU Bayern) and State Institute for the Environment of Baden-Württemberg (LUBW). Retention times for the individual LC-HRMS methods were synchronised via a spline-based retention time model [78]. As a general rule, a true positive detection needed to be confirmed with two out of three replicates and the presence of the internal standard. The normalised peak area for each substance in each measurement was calculated as follows:

$$normalised\ peak\ area = \frac{peak\ area\ (analyte)}{peak\ area\ (internal\ standard)}$$

Arithmetic and geometric means, as well as the relative standard deviation (RSD), were calculated for all replicates. If the RSD exceeded 100%, the replicate with the highest deviation was removed; if only two replicates were available and the RSD was > 100%, both were excluded. For substances with multiple adducts, the most frequent adduct with the highest normalised peak area was selected for use throughout the dataset (see Additional File 2).

Substances from the CSL were merged to the market list and their legislative category (see EU market list). As the CSL integrated spectra from different preceding research projects, it included many substances not covered by legislations, such as transformation products (TP) and laboratory research substances. Therefore, further substance information was obtained from the US EPA Chemical and Products Database (CPDat v4.0 product composition data [79]), metabolites of and substances related to HMP/VMP were identified based on a dataset by [80]. Next, the EU Prior Informed Consent Regulations (EU, 2012) [81], for severely restricted or banned substances, was assessed. Last, a substring search was performed using substance names as search queries to identify substances structurally related to those on the market list, e.g. intermediates, transformation products or metabolites; the positive matches were then checked manually.

The spectral library comprised 1721 unique substances, 1263 substances were categorised into the following groups: Industrial Substances, Food and Feed, HMP/VMP, Cosmetics, Biocidal Products/PPP. These groups include registered and approved substances, but also banned, restricted and no longer approved substances. Substances which could not be categorised using any of the named sources were classified as Other (see Additional File 1).

As many substances are registered under multiple legislations, a simplified classification according to a hierarchical scheme (PPP/Biocidal Products > HMP/VMP > Cosmetics > Industrial Substances > Food and Feed) was applied to analyse the SPM mixture across all sampling sites. This approach was used to avoid multiple counting of legislation and to identify the main route of exposure to the environment (Fig. 1). In cases where a substance has the status banned, restricted or no longer approved in a higher-level group but is registered or approved in a lower-level group, the status takes precedence over the legislative hierarchical scheme. The hierarchy was applied consistently across all substances to avoid multiple counting and to ensure comparability between sites. Importantly, this one-to-one assignment was used exclusively for aggregate mixture analyses. In analyses focusing on individual substances, all relevant legislative registrations were considered and separately reported, if applicable. Although assigning each substance to a single main legislative category may not adequately reflect real-world multi-use patterns of substances, this approach has been chosen for pragmatic reasons in this evaluation.

Data analysis

The map illustrating the sampling sites (Fig. 1) was created in QGIS version 3.28.7 [82]. Quality checks of the NTSPortal data and all processing steps regarding the EU market list were conducted in Python [83]. Data analysis of the NTSPortal data was performed with R version 4.4.3 [84] using Wilcoxon-signed rank test and effect size (wilcox.test(), wilcox_effsize()), McNemar's test (mcnemar.test()), PERMANOVA (adonis2()), and indicator species analysis (multipatt() using "IndVal.g"). To evaluate changes in presence-absence for individual substances, McNemar tests were conducted for each detected substance. Raw p-values were adjusted for multiple testing using the Benjamini–Hochberg False Discovery Rate procedure to control the risk of Type I errors. While some stations are located along the same river and may not be fully independent, spatial structuring was explicitly assessed in a two-factor PERMANOVA with Station and Year as factors. Strong spatial effects were observed, indicating that catchment-specific differences dominate mixture composition. Given the high R^2 for spatial effects and the presence-absence focus of the data, nested or explicit spatial correlation models were not applied.

To check for mixture changes across the entire dataset multivariate homogeneity of group dispersions was assessed with betadisper() and ANOVA. Further, Jaccard

distance was calculated and visualised in a non-metric multidimensional scaling plot (vegdist(), metaMDS()).

Temporal trends in annual geometric mean normalised peak areas were analysed using generalized additive models (GAMs) with mgcv [85], including *river* as a categorical factor, and residuals were checked with DHARMa [86]. Detailed information on model specifications, distributional assumptions, and selection criteria is provided in Additional File 1. Rolling means of daily water samples were calculated using rollmean() with a 7-day window. Interpolation was not applied for data gaps exceeding 7 days.

Results and discussion: examples from regulatory practice

To demonstrate the potential of the German NTSPortal in supporting chemicals management, we characterised the spatial and temporal distribution of the chemical mixture in the riverine samples, followed by selected use cases that relate to EU environmental, emission, and different chemical legislations.

Spatial distribution of chemical mixtures

Data from the German NTSPortal supported comparative assessment of chemical mixtures across three sampling programmes: Rhine river water at Koblenz (daily samples over a period of 6 years), water from rivers and streams in Saxony (individual sampling campaign), and SPM from the German ESB (annual samples, long-term programme). Out of 1721 substances included in the CSL, 855 substances (approximately 50%) were detected in at least one sample, confirming the widespread presence of micropollutants in rivers. Of these, 247 substances (29%) occurred in all three datasets whereas 142 (17%), 96 (11%) and 75 (9%) were unique to Saxony water, Koblenz water, and SPM samples, respectively (see Additional File 1 and Additional File 2). HMP/VMP, representing a rather polar substance group [87–90] within the CSL, exhibited a balanced distribution across matrices, with 33% (214, Koblenz water), 29% (167, Saxony water), and 30% (125, SPM) of all substances detected in these samples. These results indicate that substance polarity alone does not determine matrix-specific occurrence. Instead, environmental and anthropogenic factors—such as higher waste water proportions in the dataset from Saxony [74] or episodic emissions in Koblenz—appear to be the predominant factors rather than substance polarity alone.

Recent HRMS target and NTS screening studies [16, 91–93] reported hundreds of detections at Schymanski level 1, but the number of substances detected simultaneously in individual environmental samples was considerably lower. For example, [91] screened for 610 substances and reported 504 level 1 identifications in surface waters, but only in 1% of the samples more than 200 substances were detected. Similarly, our study found 855 substances in the NTSPortal dataset overall, but annual means per sampling site were lower: 475 in Saxony water (mean 255 per station), 311 in Koblenz, and 358 in SPM (mean 187 per station). These detection rates exceed prior reports and are expected to rise with the expanded CSL and additional NTS data from more comprehensive analytical techniques across additional regions. Thus, while aggregated detection counts are high, they do not necessarily represent individual stations, reinforcing that screening interpretations must consider the spatial resolution of sampling.

Temporal changes in mixture composition

Long-term mixture changes were assessed for the German ESB SPM samples. Detected substances per station over the last two decades ranged from 131 at the Danube (D1) to 220 at the Saar (S2) and 225 at the Rhine (R3 and R4) (Fig. 1). Wilcoxon signed-rank tests revealed no statistically significant change in the number of substances between earliest (2005, 2006, 2009) and latest (2022) sampling ($V = 62$, $p = 0.26$). The median difference across stations was −2 with a small effect size (Wilcoxon $r = 0.32$), indicating stable long-term conditions despite marked spatial variability among stations (see Additional File 1). This spatial variability likely reflects catchment-specific environmental and anthropogenic influences such as hydrological regime, sediment properties, land use, and population density [91, 94–96].

Temporal chemical mixture dissimilarity (presence–absence data) was analysed for the eleven sampling sites which had an identical start and end year (2006 and 2022). Pairwise dissimilarities based on presence–absence across the SPM sites revealed stronger deviations from multivariate normality in 2022 (Henze-Zirkler test (HZ) = 0.743, $p = 0.024$) than in 2006 (HZ = 0.449, $p = 0.214$), indicating a greater influence of more extreme or atypical samples. Gained and lost substances between 2006 and 2022 were identified based on presence–absence data and are summarised in Additional File 2.

Non-metric multidimensional scaling (NMDS) based on Jaccard distances showed that mixture composition changed most strongly across years at Mulde and at the Rhine sites Weil am Rhein (R1) and Koblenz (R3). R1 consistently clustered as an outlier, reflecting a distinctly different chemical profile over time in the upper Rhine (see Additional File 1). When pooling across all sites, overall detection frequency for 369 substances was not significantly different between the 2 years after controlling for multiple comparisons using the Benjamini–Hochberg False Discovery Rate correction (adjusted

p-values ≥ 0.05). Dispersion did not differ between years (McNemar test, F = 0.59, p = 0.45). Two-factor PERMANOVA identified strong spatial effects (F = 9.04, R^2 = 0.89, p = 0.001), but no temporal trend (F = 0.97, R^2 = 0.05, p = 0.48), confirming that geography, not time, determined mixture composition. While several stations are located along the same river, the strong spatial signal captured by PERMANOVA indicates that catchment-specific differences dominate chemical patterns, supporting the interpretation of station-level effects.

Indicator species analysis (IndVal.g, 999 permutations) for the dataset of 2006 and 2022 identified eight substances with significant correlations to one of the 2 years (p < 0.05). For 2006, trimethoprim (IndVal = 0.905, p = 0.001), clarithromycin (0.763, p = 0.035), and cybutryne (0.674, p = 0.037) were strong markers—mostly absent by 2022, reflecting effectiveness of measures, e.g. the EU-wide ban of cybutryne in ship coatings [97]. In contrast, in 2022, sitagliptin (IndVal = 1.000, p = 0.001), ranolazine (0.853, p = 0.001), aliskiren (0.783, p = 0.038), pantoprazole sulfide (a pantoprazole metabolite) (0.763, p = 0.022), and dronedarone (0.739, p = 0.017) were dominant; their emergence followed approval as human pharmaceuticals between 2007 and 2009 [98–102]. The limited set of indicator substances, pointing to overall high temporal stability in the mixture, confirms the strong influence of space over time. These outcomes confirm prior findings from a target study of small temporal change in pharmaceuticals present in the Rhine from the late 1990s through 2006 [103], suggesting that persistent mixture composition extends beyond pharmaceuticals and mixtures are older and more temporally stable than often considered.

HRMS NTS data in environmental, emission and chemical legislation

Environmental exposure data are crucial for prioritizing substances in water monitoring under the Environmental Quality Standards Directive 2008/105/EC [104]. In contrast, chemical legislations rely on modelling exposure levels in prospective environmental risk assessment without re-evaluating their plausibility with monitoring data after market approval. Linking real-world exposure evidence to regulatory decision-making is essential to overcome fragmentation of environment, emission and chemical legislations [105]. Here, we give examples how retrospective screening with NTSPortal data can support the different sectors.

Environmental legislation—EU WFD and watch list

The NTSPortal data from water (Koblenz and Saxony) and SPM samples were analysed to assess their potential for supporting substance prioritisation under the Environmental Quality Standards Directive [104] of the Water Framework Directive [8]. Regulatory prioritisation for monitoring depends largely on the frequency of detection of a candidate substance in the environment from classical target studies [106]. To address data gaps, a watch list mechanism was formally introduced in 2013 [107, 108], providing updated exposure datasets for selected substances every 2 years. The current fifth European Watch List [109, 110] comprises twelve substance groups containing 29 substances, 24 of which are included in the CSL. Of these, 12 substances were not detected at any water or SPM station. Their absence likely reflects low environmental concentrations, high polarity favouring the aqueous phase (e.g., metformin), or rapid environmental transformation (e.g., N-(1,3-dimethylbutyl)-N-phenyl-p-phenylenediamine (6PPD) to 6PPD-quinone [111]). Accordingly, 12 of the Watch List substances were detected within the NTSPortal data, with ten substances found both in SPM samples and in water samples from Koblenz and eight substances present in water samples from Saxony, indicating widespread distribution. The temporal trend of SPM data for all new Watch List substances with sufficient data points to conduct trend analysis revealed that three substances increased significantly (GAM Gamma/Tweedie: p(year) < 0.05, slope = 0.01–0.03), two remained unchanged (GAM Gamma/Tweedie: p(year) < 0.05 and p > 0.05, slope = 0.00) and four substances decreased significantly (GLM/GAM Gamma/Tweedie: p(year) < 0.05, slope = −0.28 to −0.01) over the last two decades (see Additional File 2).

As a specific example, the tyre additive 6PPD and its TP 6PPD-quinone were added to the fifth EU WFD Watch List after [111] revealed their acute toxicity to *Oncorhynchus kisutch*. To retrospectively assess long-term trends, the two substances were included in the CSL, and 6PPD-quinone was detected in SPM samples from 8 of 13 stations along the Rhine, Saar and Elbe, most of which were collected before tyre abrasion was recognised as an environmental concern. It has been consistently present since 2005, showing a slight decreasing trend (generalized linear model (GLM): p(year) = 0.05, slope = −0.01), indicating that environmental exposure has been largely stable. It suggests that the rapid increase in research activity, reflected by a strong increase in publications on these substances between 2020 and 2025 (over 2900 results in Google Scholar), does not necessarily reflect increases in environmental exposure levels. In contrast, 6PPD-quinone was not detectable in any of the water samples from Saxony and only occasionally (1.3%) in samples from Koblenz. This example illustrates how the NTSPortal, as a digital environmental specimen bank, can, in combination with physical ESB samples,

support regulatory monitoring. Various authors have suggested a link between heavy rainfall and the presence of substances from tyre abrasion in surface waters [111–114]. Figure 2 shows the occurrence of tyre abrasion-related substances in surface water and SPM in relation to precipitation. While 6PPD-quinone was occasionally detected in the water phase, no consistent relationship with precipitation events was apparent. In contrast, 6PPD-quinone was more reliably detected in SPM, suggesting that this matrix provides a more stable indication of riverine exposure when water-phase levels are low or variable. Hexamethoxymethylmelamine (HMMM), another substance linked to tyre abrasion, exhibited different temporal patterns and also showed no clear connection to heavy precipitation events. These observations suggest that the environmental occurrence of tyre abrasion-related substances is influenced by multiple factors and is not easily explained by precipitation or the source category tyre abrasion alone, highlighting the value of multi-matrix, long-term monitoring for understanding exposure dynamics.

This case study illustrates how established and upcoming NTS portals can support prioritisation with trend information on candidate substances across Europe once sufficient data has been stored in the coming years, for example, within the Water Framework Directive. The detection of 12 Watch List substances demonstrates that most of these substances can be readily detected by NTS across different matrices and regions, and the data can serve as an efficient screening tool, reducing the need for extensive routine target analyses and freeing analytical resources for substances that are more difficult to measure and require specialised target methods.

Emission legislation—urban waste water treatment directive (UWWTD)

The revised Urban Waste Water Treatment Directive (UWWTD, EC 2024/3019) [117] updated the requirements for monitoring and reducing micropollutants in urban waste water, with implementation mandated by 2027. Article 9 introduces extended producer responsibility, requiring industrial sectors largely contributing to these pollutants—primarily the pharmaceutical and cosmetics industries—to financially contribute. With the Directive, thirteen indicator substances were selected to monitor the effectiveness of upgrading waste water treatment plants with quaternary treatment, with the CSL providing coverage for all of these substances (see Additional File 2). 4- and 5-methylbenzotriazole are listed as individual indicator substances in the Directive. However, in this study, the two regioisomers could not be analytically distinguished. Therefore, any detection of 4-methylbenzotriazole was reported as representing both 4- and 5-methylbenzotriazole and vice versa. Ten substances were detected in SPM, four with significant increasing trends (GAM Gamma/Tweedie: $p(year) < 0.05$, slope = 0.02–0.11), i.e. amisulpride, citalopram, metoprolol, and venlafaxine, five with a marked decrease (GAM Gamma/Gaussian: $p(year) < 0.05$ and one substance $p(year) > 0.05$, slope = −0.02 to −0.01), and one maintaining a consistent level (GAM Gamma: $p(year) < 0.05$, slope = 0.00). All 13 indicator substances appeared consistently in water samples from Koblenz and Saxony, demonstrating their widespread environmental occurrence.

Beyond the 13 selected indicators, the CSL contained 548 additional substances related to the scope of the revised UWWTD (HMP/VMP, Cosmetics) with detection rates of 244 (Saxony water), 196 (Koblenz water), and 160 (SPM). In all three matrices, 99 substances were ubiquitously present. Considering all years and all SPM stations, pharmaceuticals and cosmetics accounted for the largest share of detections (37–47%, Fig. 1). In the rivers Saar, Elbe, Mulde and Saale, the number of detected substances increased until the mid-2010s, after which it declined again to almost its original level. In the Rhine, on the other hand, after constant values in previous years, there was a decline in the number of substances detected, while the numbers for the Danube remained stable over the entire period (Fig. 3). A comparable temporal trend was observed for European freshwater invertebrate communities [118]: several metrics improved until the 2010s, which the authors related to water quality measures (e.g., waste water treatment upgrades and habitat restoration), followed by a plateau attributed to persistent substances—consistent with the stability of substance groups observed in this study. The lowest detection counts were observed in Danube and Mulde, while the other rivers clustered with higher detection counts.

We evaluated the temporal changes in the presence of pharmaceuticals and cosmetics in the same way as before for all CSL substances (Fig. 4). Indicator Type Analysis (IndVal, 999 permutations) identified six pharmaceuticals as being significantly associated with one of the years ($p < 0.05$). As previously for all CSL substances, the test also revealed only a small number of indicator substances in this case. In 2006, trimethoprim (IndVal = 0.905, $p = 0.001$) and clarithromycin (0.763, $p = 0.028$) were the main indicators, while in 2022, sitagliptin (1.000, $p = 0.001$), ranolazine (0.853, $p = 0.001$), aliskiren (0.783, $p = 0.031$), and dronedarone (0.739, $p = 0.011$) dominated. Clarithromycin is among the official UWWTD indicators and largely disappeared by 2022, indicating reduced environmental exposure. The data confirm earlier reports on the contribution of pharmaceuticals to riverine chemical mixtures in

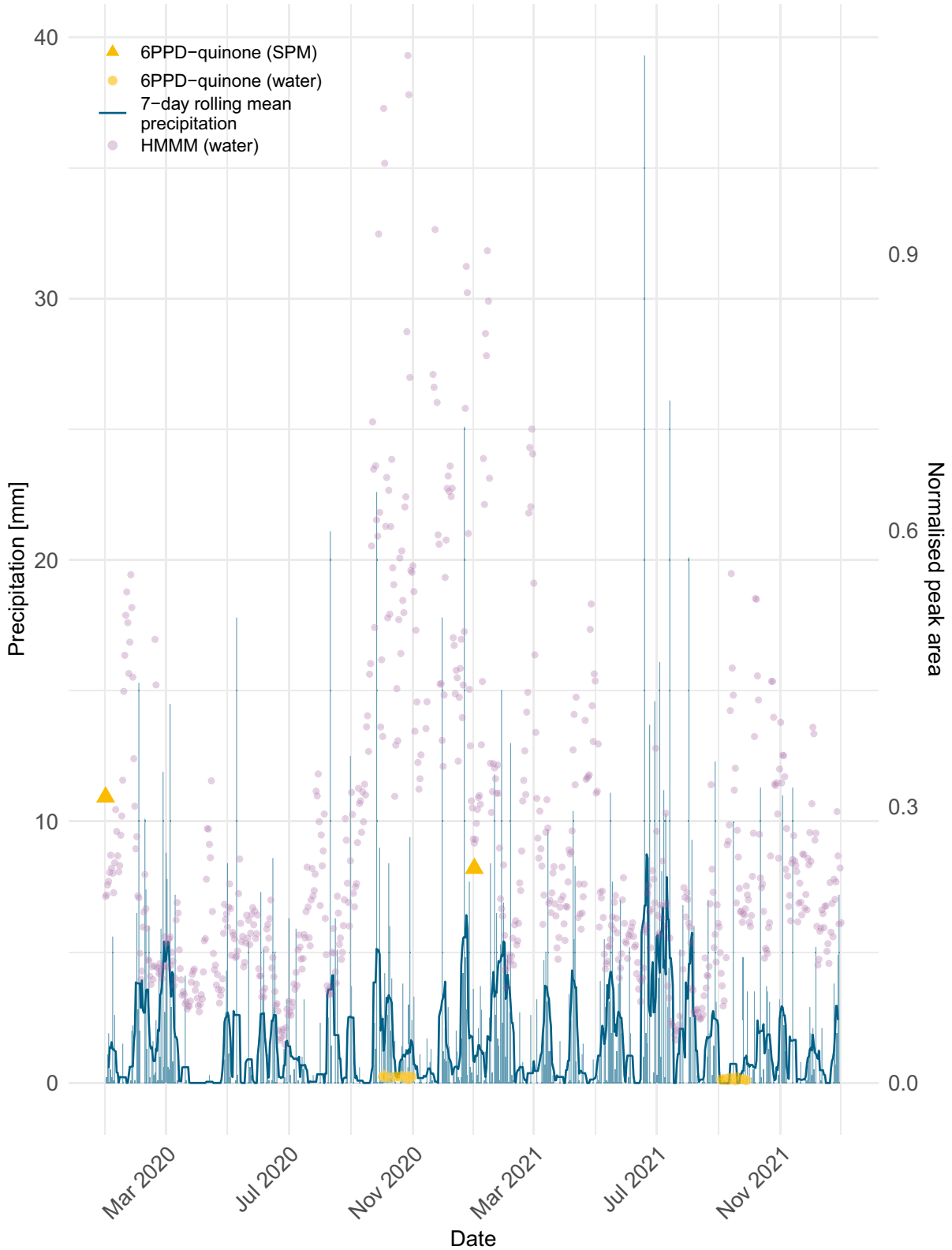


Fig. 2 Precipitation [mm] at Andernach (near Koblenz) and normalised peak areas of 6PPD-quinone and HMMM in samples from Koblenz, Rhine from 2020 to 2022. Blue bars: daily precipitation, blue line: 7-day rolling mean of precipitation. Orange points: daily 6PPD-quinone (water); orange triangles: 6PPD-quinone (annual SPM); purple points: daily HMMM (water). Precipitation data: Deutscher Wetterdienst, Station 161 [115, 116]

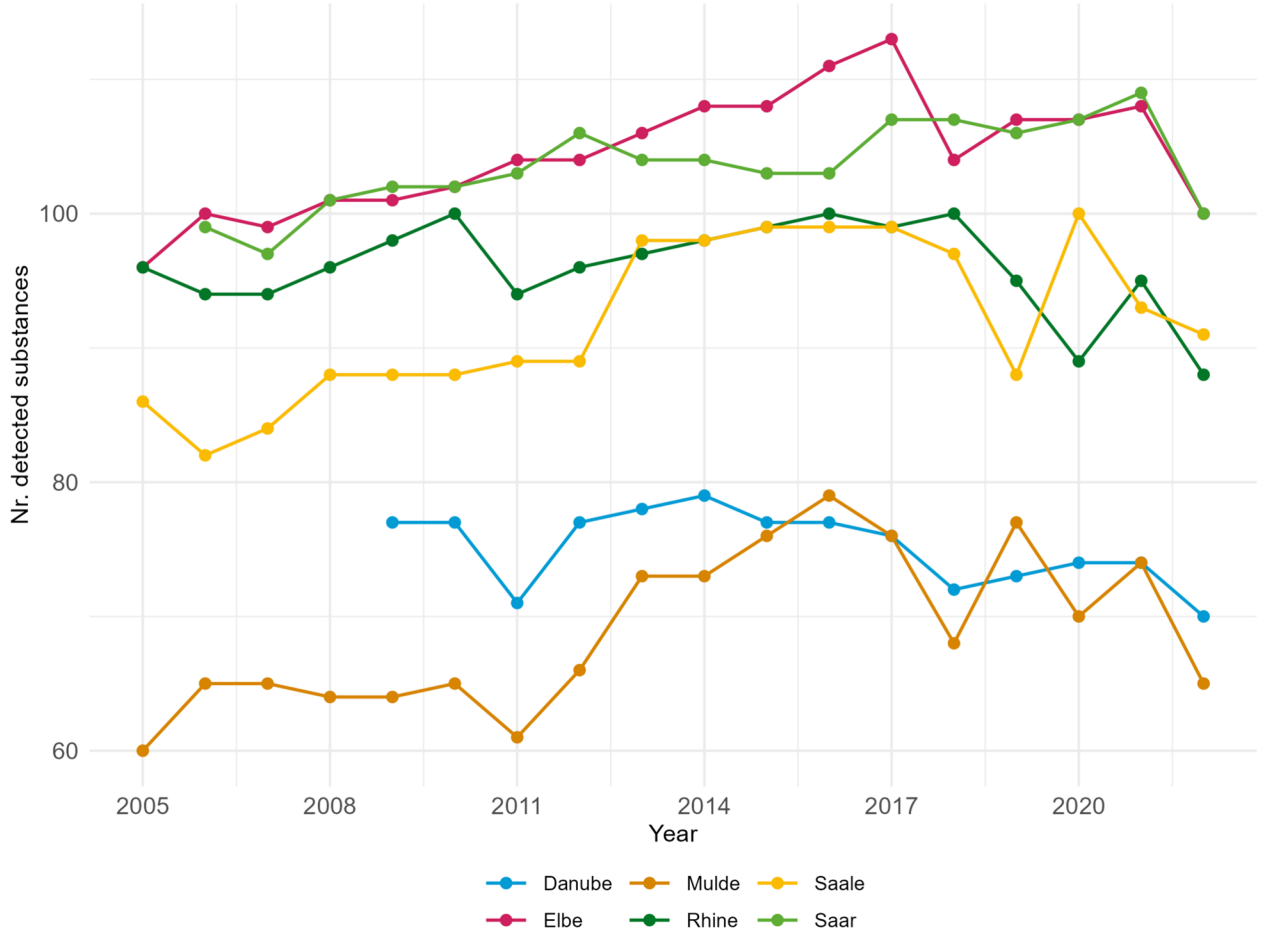


Fig. 3 Number of detected HMP, VMP, and Cosmetics including related substances in annual SPM samples from the Danube (D1, D3), Elbe (E1, E2, E4, E5), Mulde, Rhine (R1, R3, R4), Saale, and Saar (S1, S2) rivers over time. Note that sampling along the Saar river started in 2006 and along the Danube river in 2009

Germany [93, 119–121]. Previously reported trends from target analysis for 61 substances related to pharmaceuticals in archived SPM samples from the Saar and Rhine river systems have been described [75, 122]. The NTSPortal's broader scope in terms of number of analytical standards in the CSL, sample matrices and sampling sites has led to the detection of more substances in comparison.

NMDS values based on Jaccard distances focusing on pharmaceuticals and cosmetics revealed more distinct temporal and spatial patterns than compared to the analysis for the entire CSL mixture (see Additional File 1): Station E5 showed more year-to-year distance, Saar stations S1/S2 greater similarity, and R1 replicated the overall mixture pattern. In 2006, mixture dispersion and variability were greater than in 2022. This approach helped to validate indicator substances, e.g. for UWWTD and contextualises them among substances with similar uses.

Emission legislation—industrial emissions directive

The Rhine is located in Europe's most industrialised catchment area, with segmented industrial sectors along the river [123, 124]. While traces from diffuse sources such as urban waste water are increasing along the Rhine as the number of inhabitants grows, contradictory trends may indicate point sources from production. As an example, [75] attributed the unexpected decline in concentrations of the antidepressant fluoxetine in SPM samples along stations R1, R2, and R3 on the Rhine to upstream industrial emissions from the pharmaceutical industry. We found the same spatial trend in the NTSPortal data where fluoxetine was detected at higher levels at R1 compared to R3 and five additional stations from other rivers despite an overall increasing temporal trend (GAM Gamma: $p(\text{year}) < 0.05$, $\text{slope} = 0.01$). Likewise, mefloquine, a fluorinated pharmaceutical used for malaria prevention and treatment, showed an unusual exposure pattern in

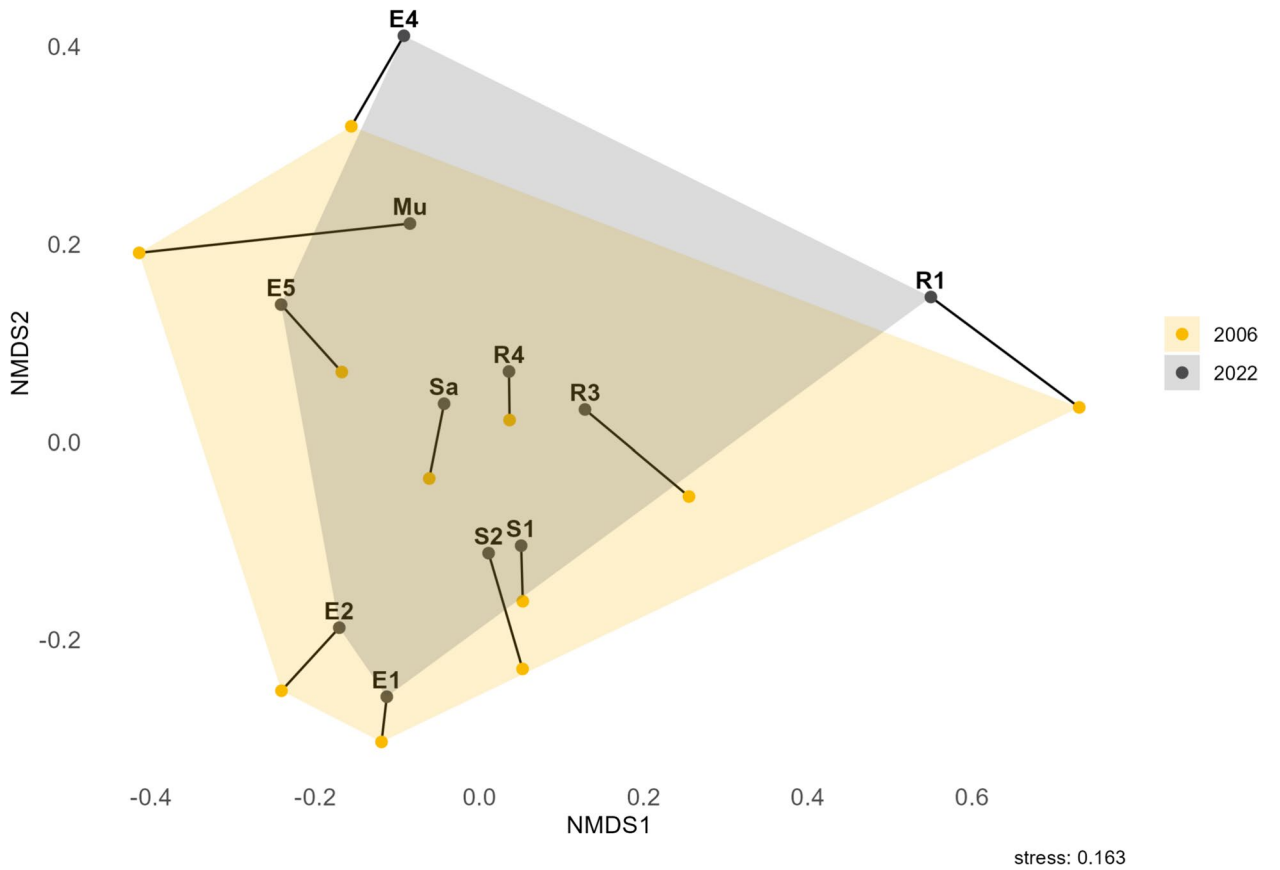


Fig. 4 Non-metric multidimensional scaling (NMDS) plot of Jaccard distances of HMP, VMP, Cosmetics and related substances detected in annual SPM samples from eleven stations (E1, E2, E4, E5, Mu, R1, R3, R4, S1, S2, Sa) in 2006 (orange) and 2022 (grey). Dashed lines connect the same stations in different years. Shaded areas indicate the outline of station points for each year, showing overall group distribution. Stress value = 0.163

the SPM NTSPortal data, as it was detected along the Rhine at R1 from 2005 to 2020, while detections downstream at R3 and R4 had already ended in 2016. Since Germany is not a malaria region and the manufacturer (located upstream R1) withdrew its marketing authorisation in 2016 with a 2-year transition period [125, 126], the gradual disappearance of mefloquine from the Rhine with decreasing distance from a point source indicates industrial emissions.

In a target study, [127] analysed organic UV filters in archived SPM samples from the river Rhine and found a strong increase of diethylaminohydroxybenzoylhexyl benzoate (DHHB) at R3 compared to R1 (upstream) and R4 (downstream) since 2017, indicating industrial emission sources. The NTSPortal data confirmed the point source theory with data from additional river sampling sites, which also showed an increase (GAM Tweedie: $p(year) < 0.0001$, slope = 0.39), albeit at lower levels, which can be explained by the widespread use of DHHB-containing sunscreens by consumers.

A prioritisation strategy to identify contaminants in an LC-HRMS NTS dataset from a Rhine monitoring site close to R1 was developed by [13], identifying several industrial emission-related substances as major contributors to the contamination load. In the present dataset, 2-[(dimethylamino)methyl]benzonitrile—a substance newly identified by [13] that ranks among the top 40 with an annual load of ca. 1 t near R1—was detected at all sampling sites (R1, R3, R4) along the Rhine.

Similarly, [128] identified emission patterns from the production and use of triphenylphosphonium compounds near individual SPM sampling sites on the Rhine (R3) and Elbe (E2, E4). Data from other sampling sites included in the NTSPortal reinforced the suspicion that these are the main production and use areas for triphenylphosphonium compounds and other quaternary ammonium compounds in Germany.

The data show that modern environmental NTS analyses can identify the industrial production of certain individual substances in rivers. With the addition of wastewater samples from industrial plants and municipal

sewage treatment plants, NTS Portals could take an even bigger step forward in distinguishing point sources from diffuse inputs.

Chemical legislation—cosmetic products regulation

Of the 42 substances listed in the CSL as cosmetic ingredients, 26 were found in the NTSPortal data. Specifically, 18 were detected in water from Saxony, 17 in water from Koblenz, and 23 in SPM. Based on the NTSPortal data we determined whether use restriction measures for climbazole were effective, which is primarily used as an anti-dandruff agent and preservative in cosmetic products [129]. Due to concerns about human health, maximum levels for cosmetic products were introduced in the EU Cosmetic Regulation [64] in 2008 and further reduced in subsequent amendments to annexes III and V of the regulation [130]. Under the REACH Regulation, which is responsible for the environmental aspects of cosmetics, substance evaluation confirmed widespread use, endocrine disruption and aquatic toxicity [131, 132]. Climbazole has been detected at all SPM sampling sites since 2005 (GAM Gamma: $p(year) < 0.0001$, $slope = -0.28$, Fig. 5). Underlining the effectiveness of the two successive regulatory measures, normalised peak areas in SPM samples declined from 2008 onwards, plateaued between 2013 and 2017, and have continued to decrease since then, with levels converging across all stations. In Koblenz, there were very few detections in the water phase (2.2% of all time points) and no detections at all at the measuring stations in Saxony.

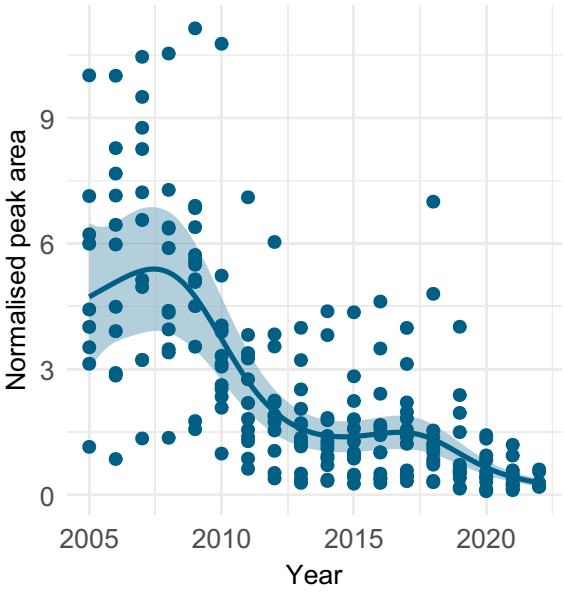


Fig. 5 Normalised peak areas of climbazole in SPM samples from the Elbe (E1, E2, E4, E5), Mulde (Mu), Rhine (R1, R3, R4), Saale (Sa), Saar (S1, S2), and Danube (D1, D3) rivers. Blue points represent individual annual samples. Blue line shows the overall GAM Gamma fit with a weighted smooth and 95% confidence interval ($p(year) < 0.0001$, $slope = -0.28$). For river-specific contributions see Additional File 1

Chemical legislation—REACH regulation and national centre for micropollutants

Out of approximately 300 substances listed in the CSL as industrial chemicals under REACH (EC 1907/2006) [59], 177 were detected in the NTSPortal data. Specifically, 128 were found in water samples from Saxony, 143 in water samples from Koblenz, and 92 in SPM samples. The German Centre for Micropollutants (SZB) was founded to comprehensively and proactively protect water bodies and drinking water production in Germany in cooperation with relevant stakeholders [133]. The SZB prioritised 27 substances and one substance group (sartans) as relevant micropollutants. Of these, 23 substances were included in the CSL and 15 were detected in at least one matrix. The CSL comprised 12 sartans, including their metabolites and TP, of which 10 were detected in at least one matrix of the NTSPortal dataset. Benzotriazole, used as a corrosion inhibitor in metal processing and cooling systems, and as an additive in dishwashing detergents, was also detected [134, 135]. Due to its persistence and mobility in water, the SZB began moderating a voluntary phase-out of benzotriazole in household dishwashing detergents in 2022 [136] and is currently identifying suitable alternatives.

We made use of the NTSPortal data to support the SZB with retrospective trend data and to determine whether voluntary use restrictions for benzotriazole had an effect. In SPM samples, 1H-benzotriazole and its TPs 4- and 5-methyl-1H-benzotriazole were detected at 11 of 13 sampling sites with levels peaking around 2017 (see Additional File 1). One additional TP, 4-hydroxy-1H-benzotriazole, was detected in water samples from Koblenz and Saxonian rivers and water bodies of varying sizes. Ongoing NTSPortal monitoring will reveal whether measures to reduce aquatic exposure are effective.

Chemical legislation—plant protection and biocidal products regulation

A total of 363 substances were listed in the CSL and marketed in PPP and/or Biocidal Products, of which 141 were detected in the NTSPortal data. More specifically, 113 were detected in water from Saxony, 81 in water from Koblenz and 48 in SPM.

We made use of the NTSPortal data to determine whether the cessation of the marketing of carbendazim in PPPs and Biocidal Products reduced their environmental exposure. The EU authorisation for carbendazim as a fungicide in cereal cultivation [137] expired at the end

of 2014, with a grace period until mid-2016 [138]. It was detected at 7 of 13 SPM sites from 2005 to 2022 (GAM Gamma: p(year) < 0.0001, slope = −0.01) and declined markedly after 2017 (Fig. 6). In water samples from Koblenz, it decreased and was mostly undetectable by 2022. This decline indicates effective PPP risk management, while restrictions for most biocidal uses followed in 2019 [139] and likely reinforced the trend. In contrast, the continued use as a REACH preservative in paper and textiles remained permitted but contributed only marginally to exposure compared to the former use in PPP and Biocidal Products.

Another example is the non-systemic fungicide fludioxonil, which was exclusively detected in SPM samples from only two Rhine stations, suggesting common local exposure sources (see Emission legislation—Industrial Emissions Directive). The substance is mainly used in PPPs to treat seeds (seed coating) and fruit (after harvesting) against fungal diseases [140]. Environmental exposure is less likely than for other PPP used directly in agriculture. In recent years, fludioxonil levels have declined (see Additional File 1) and will likely continue as its approval expires in 2026 [138] due to endocrine-disrupting properties [140].

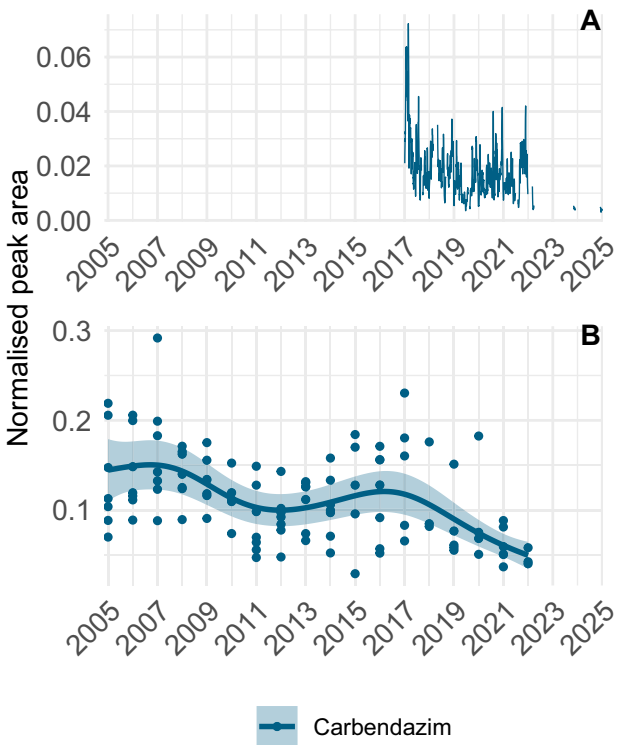


Fig. 6 Normalised peak areas of carbendazim in (**A**) surface water at Koblenz (data available since 2017), expressed as a 7-day rolling mean, and SPM samples (**B**) from the Elbe (E1, E2, E4), Mulde (Mu), Rhine (R3, R4), and Saale (Sa) rivers. Blue points indicate individual annual measurements, while the lines represent the GAM Gamma fit (p(year) < 0.0001, slope = −0.01) with a weighted smooth and associated 95% confidence interval

Azole-fungicides are, depending on their intended use, regulated as PPP or Biocidal Product. NTSPortal data provided an overview for ecosystem and human health assessment on azole-fungicides. Systemic azole-fungicides are applied directly at large scales to agricultural lands [141–143]. Addressing resistance development, experts and EU regulatory bodies have urged to better understand the environmental presence and the impacts of these fungicides [144, 145]. Retrospective HRMS screening was applied by [39] to archived data and confirmed their widespread occurrence in both the water column and sediments. Recently, ten azole-fungicides, including 7 still marketed PPP, were added to the 4th and 5th EU Watch List [110, 146] and are all included in the CSL. Propiconazole and epoxiconazole were found in all matrices. In total two, three, and four substances were found in NTSPortal data for water samples from Saxony, Koblenz, and in SPM, respectively. For the substances in SPM samples with a sufficient number of data points for trend assessment, two showed decreasing trends (climbazole and propiconazole, GAM Gamma: p(year) < 0.05, slope = −0.28 and −0.01), while one showed no trend (epoxiconazole, GAM Gamma: p(year) < 0.05, slope = 0.00) over the last two decades.

According to the EFSA report [144], 18 azole-fungicides were predominantly sold between 2010 and 2021, with tebuconazole being the most widely sold. In total, 16 of these substances were included in the CSL, while prothioconazole was not; however, its major metabolite prothioconazole-desthio was included [147, 148]. Overall, ten substances related to azole-fungicides, including prothioconazole-desthio, were detected in water and/or SPM, whereas eight were present in SPM only. For those with sufficient data for trend assessment, significantly decreasing trends (climbazole and propiconazole, GAM Gamma: p(year) < 0.05, slope = −0.28 and −0.01), no trend (epoxiconazole and prothioconazole-desthio, GAM Gamma: p(year) < 0.05, slope = 0.00), and an increasing (tebuconazole, p(year) > 0.05, slope = 0.01) trend were observed.

These examples illustrate how NTSPortal data can be used to support One Health strategies with unprecedented data in addition to chemicals management.

Chemical legislation—human and veterinary medicinal products

A total of 479 substances were listed in the CSL as related to HMP (2001/83/EC) [62] and VMP [63] (EU 2019/06). Of these, 259 were detected in environmental data from the NTSPortal. More specifically, 214 were detected in

water from Saxony, 167 in water from Koblenz and 125 in SPM.

The NTSPortal data were used to provide an overview on environmental trends arising from therapeutic and pharmacological innovation. The antidepressant citalopram (Anatomical Therapeutic Chemical (ATC) code: N06AB04) has been frequently detected in SPM samples. Trend analyses revealed a significant increase in levels of both the parent substance (GAM Gamma: $p(year) < 0.0001$, slope = 0.11) and its metabolite N-desmethyl-citalopram (GAM Gamma: $p(year) < 0.0001$, slope = 0.03, Fig. 7) over time. In the late 2010s, the levels began to decline. Increasing levels of citalopram were consistent with those observed for other antidepressants, such as venlafaxine (GAM Gamma: $p(year) < 0.0001$, slope = 0.06). In addition to citalopram, other fluorinated pharmaceuticals, including fluoxetine, flecainide, sitagliptin, flusilazole, and melperone were also detected in the SPM data. In total, 26 fluorinated HMPs and/or VMPs were detected in at least one matrix, including 6 neuroactive substances (ATC group N). Degradation studies have shown that fluorination can increase the persistence of pharmaceuticals in waste water treatment and the environment [149, 150]. Notably, sitagliptin, fluoxetine and flecainide meet the Organisation of Co-operation and Development (OECD) definition of PFAS [151], which is the basis for the proposed EU restriction on PFAS-containing groups [152]. The use of PFAS pharmaceuticals in the EU was estimated to increase by 3.4% per year in 2019 [153], and although these pharmaceuticals are currently exempt from the scope of the use restriction, SPM data indicate they contribute substantially to the total PFAS load in rivers [154].

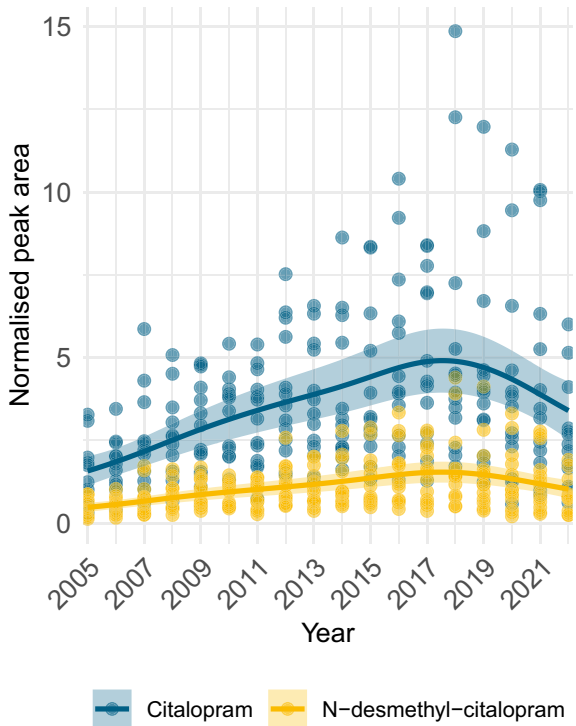


Fig. 7 Normalised peak areas of citalopram (blue) and N-desmethyl-citalopram (orange) in SPM samples from the Elbe (E1, E2, E4, E5), Mulde (Mu), Rhine (R1, R3, R4), Saale (Sa), Saar (S1, S2), and Danube (D1, D3) rivers. Points indicate individual annual measurements, while the lines represent the GAM Gamma fit with a weighted smooth and associated 95% confidence interval. Citalopram: $p(year) < 0.0001$, slope = 0.11; N-desmethyl-citalopram: $p(year) < 0.0001$, slope = 0.03. For river-specific contributions see Additional File 1

Furthermore, the NTSPortal was used to support regulatory decision-making with background levels for veterinary medicines. Limited data exist on aquatic exposure from VMP in food-producing [155, 156] and companion animals [157–159]. In 2025, the European Medicines Agency (EMA) assessed environmental risks when considering changing flubendazole authorisation for companion animals from prescription-only to prescription-free. German NTSPortal data showed the substance was only detected at two Saar River stations near the French border (decreasing trends, GAM Gamma: $p(year) < 0.05$, slope = −0.01). The EMA concluded exposure was mainly from human medicinal use in France ('Fluvermal', unauthorised in Germany), while exposure contribution from companion animal risk remained negligible. This represents the first known use of non-target data in pharmaceutical risk assessment.

Outlook and conclusion

Data from the NTSPortal provided a multi-matrix and multi-temporal characterisation of chemical pollution patterns in German rivers. While the total chemical mixture remains extensive, compositional stability and dominant spatial structuring indicated persistent anthropogenic pressures shaped by catchment-specific sources. We demonstrated that the data can be used across matrices and spatial scale to enhance the tracing of chemical footprints, to evaluate regulatory progress, and to contextualise mixture exposure across German surface waters by:

- increasing the resolution of chemical mixtures in aquatic samples by investigating a larger number of substances than in classical target monitoring with a similar level of certainty;
- providing spatial and temporal trend data for different river basins and matrices, and thereby supporting regulatory requirements in monitoring and chemicals risk assessment;
- integrating similarity-based multivariate approaches to compare and interpret chemical mixture patterns.

Digital HRMS NTS repositories such as the German NTSPortal represent an important investment in the future of water management. They can be can be systematically expanded in various dimensions:

- temporally, via continuous sample addition—such as the addition of monthly SPM samples to the NTSPortal – and temporal trend analysis;
- chemically, by including NTS data from LC-HRMS and gas chromatography (GC)-HRMS methods—GC-HRMS integration in the NTSPortal started in 2026—the continuous addition of new substances to the CSL, and the integration of HRMS NTS data from unkown screening;
- spatially, with new sampling sites and integrating new regions—for example by including further data from the state-level environmental agencies;
- and through matrix diversity, e.g., waste water, sediments, and biota.

For maximum regulatory impact, it is crucial to connect users across different legislation to enable cross-sector data use and promote integrative chemicals management, as envisaged, for example, in the EU OSOA and One Health approaches. Adherence to the FAIR data principles and improved interoperability of existing and upcoming NTS portals can further enhance digitalisation in water management. Therefore, other environmental specimen banks are encouraged to retrospectively analyse their archived samples using HRMS NTS or to make samples available to NTS portals [160].

At the same time, limitations of the NTSPortal should be acknowledged to provide a balanced perspective:

- quantification and risk characterisation: the NTSPortal currently provides presence-absence data and intra-substance peak area comparisons, but absolute concentration data are missing, limiting risk assessment options;
- coverage of chemical space: detection is restricted to substances included in the CSL and the methods currently implemented. Some substances, matrices, or analytical techniques are not yet covered. The NTSPortal cannot achieve complete chemical space coverage, though it improves upon conventional target studies;
- integration of unknowns and effect data: unknown screening and toxicity data are not yet systematically integrated, although future developments may allow quantification and predictive toxicity assessments.

Recent advances, however,—such as prioritisation [161], quantification [58] and toxicity predictions from HRMS data [162]—highlight the growing regulatory potential of NTS. Building on these advances and the continuously growing volume of data, the application of big data and AI-based tools to NTS portal data will further improve its use in regulatory applications.

Abbreviations

6PPD	N-(1,3-dimethylbutyl)-N-phenyl-p-phenylenediamine
API	Application Programming Interface
ATC	Anatomical Therapeutic Chemical code
BfG	Federal Institute of Hydrology (Bundesanstalt für Gewässerkunde)
CAS	Chemical Abstracts Service
CPDat	Chemical and Products Database
CSL	Collective Spectral Library
D1	ESB station Ulm (Danube)
D3	ESB station Jochenstein (Danube)
DIN	German Institute for Standardisation (Deutsches Institut für Normung)
DSFP	Digital Sample Freezing Platform
E1	ESB station Prossen (Elbe)
E2	ESB station Zehren (Elbe)
E4	ESB station Cumlosen (Elbe)
E5	ESB station Blankenese (Elbe)
EC	European Commission
EMA	European Medicines Agency
ESB	Environmental Specimen Bank
EU LIFE	LIFE Programme of the European Union
GAM	Generalized Additive Model
GC	Gas chromatography
GdCh	German Chemical Society (Gesellschaft Deutscher Chemiker)
GLM	Generalized Linear Model
HMMM	Hexamethoxymethylmelamine
HMP	Human Medicinal Product
HRMS	High-resolution mass spectrometry
HZ	Henze-Zirkler test
ICPR	International Commission for the Protection of the Rhine
JSON	JavaScript Object Notation
LC	Liquid chromatography
LfU	Bavarian State Office for the Environment (Bayerisches Landesamt für Umwelt)
LUBW	State Institute for the Environment of Baden-Württemberg (Landesanstalt für Umwelt Baden-Württemberg)
Mu	ESB station Dessau (Mulde)
NEN	Royal Netherlands Standardization Institute (Stichting Koninklijk Nederlands Normalisatie Instituut)
NMDS	Non-metric Multidimensional Scaling
NORMAN	Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances
NTS	Non-Target Screening
OECD	Organisation for Economic Co-operation and Development
OSOA	One Substance, One Assessment
PARC	Partnership for the Assessment of Risks from Chemicals
PPP	Plant Protection Product
QTOF	Quadrupol Time-of-Flight
R1	ESB station Weil am Rhein (Rhine)
R3	ESB station Koblenz (Rhine)
R4	ESB station Bimmen (Rhine)
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals (EC 1272/2008)
RSD	Relative Standard Deviation
S1	ESB station Güdingen (Saar)
S2	ESB station Rehlingen (Saar)
SPM	Suspended particulate matter
SZB	German Centre for Micropollutants (Spurenstoffzentrum des Bundes)
TP	Transformation product
UBA	German Environment Agency (Umweltbundesamt)
UWWTD	Revised Urban Waste Water Treatment Directive (EU 2024/3019)

VMP Veterinary Medicinal Product
WFD Water Framework Directive (EC 2000/60)

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12302-026-01368-x.

Additional file 1.

Additional file 2.

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Author contributions
ALK: formal analysis, investigation, visualisation, writing—original draft, RMW: data curation, investigation, writing—review and editing, EW: investigation, writing—review and editing, NB: funding acquisition, writing—review and editing, KSJ: data curation, investigation, methodology, software, writing—review and editing, GD: investigation, methodology, writing—review and editing, AW: resources, writing—review and editing, JK: conceptualisation, funding acquisition, supervision, project administration, writing—original draft.

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Data availability
The dataset(s) supporting the conclusions of this article is(are) available in the Zenodo repository: https://doi.org/10.5281/zenodo.18717406 and in Additional File 2. Access to the NTSPortal website (https://ntsportal.bafg.de) and API (https://elastic.bafg.de) can be provided upon request to the corresponding author or to ntsportal@bafg.de.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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