

Suspect Screening and Regulatory Databases: A Powerful Combination To Identify Emerging Micropollutants

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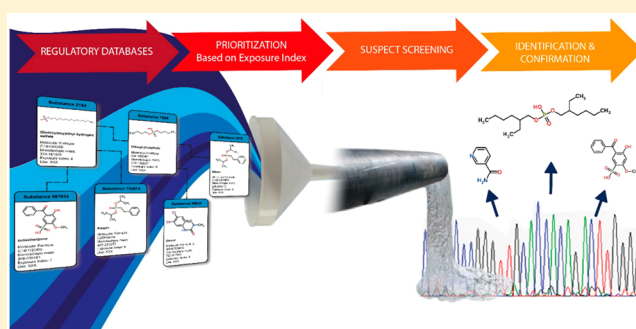
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Supporting Information

ABSTRACT: This study demonstrates that regulatory databases combined with the latest advances in high resolution mass spectrometry (HRMS) can be efficiently used to prioritize and identify new, potentially hazardous pollutants being discharged into the aquatic environment. Of the approximately 23000 chemicals registered in the database of the National Swedish Product Register, 160 potential organic micropollutants were prioritized through quantitative knowledge of market availability, quantity used, extent of use on the market, and predicted compartment-specific environmental exposure during usage. Advanced liquid chromatography (LC)–HRMS-based suspect screening strategies were used to search for the selected compounds in 24 h composite samples collected from the effluent of three major wastewater treatment plants (WWTPs) in Sweden. In total, 36 tentative identifications were successfully achieved, mostly for substances not previously considered by environmental scientists. Of these substances, 23 were further confirmed with reference standards, showing the efficiency of combining a systematic prioritization strategy based on a regulatory database and a suspect-screening approach. These findings show that close collaboration between scientists and regulatory authorities is a promising way forward for enhancing identification rates of emerging pollutants and expanding knowledge on the occurrence of potentially hazardous substances in the environment.



INTRODUCTION

The world of chemicals is very complex, with more than 100000 substances in commercial use globally. Emissions of synthetic substances into the aquatic environment pose a risk to water quality and may trigger unwanted effects.¹ The majority of regulatory and enforcement agencies responsible for water quality assume that a small number of well-known substances (e.g., priority pollutants described by the EU Water Framework Directive) are responsible for a significant share of environmental, human health, and economic risks.² However, the accuracy of this assumption is questionable since the chemicals which are regulated by official agencies represent only a tiny fraction of the chemical stressors occurring in the environment. Most potentially hazardous compounds are thus not covered by any existing water quality regulations or included in environmental screening programs. Chemical monitoring and analysis are commonly carried out for a preselected small proportion of organic contaminants, thus overlooking important site-specific and potentially hazardous substances.³ This is particularly the case with many industrial chemicals, which are systematically omitted from monitoring studies.

The latest advances in high-resolution mass spectrometry (HRMS) have initiated a new trend in analytical data processing in recent years. Targeted analytical methods are now often complemented with suspect and nontarget data acquisition and screening methods.^{4,5} In suspect-screening workflows, there is no need for reference standards until the confirmation stage, thus saving time and money and allowing the inclusion of an extensive list of substances.

Suspect screening is a complex process, and a crucial step within this is to produce smart suspect lists in order to achieve a better understanding of specific research questions. Different strategies for selection of suspects in environmental samples have been developed for various chemicals and compound classes, e.g., for registered pesticides and associated transformation products (TPs),^{6,7} pharmaceuticals,^{8–10} their predicted metabolites^{11–13} and photodegradation products,^{14–18} surfactants,^{11,14,19–22} fracking fluids,²³ predicted TPs,^{24–28} new

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psychoactive substances,²⁹ and illegal additives,³⁰ as well as for different families of compounds.^{31–40}

Ideally, when creating suspect-screening lists, all pre-existing relevant information is considered. The Swedish chemicals legislation requires manufacturers and importers to register chemical substances and products in a national product register. Chemical registration data show the identity of substances released on the market and contain information on, e.g., market availability, use pattern, and quantity used, which are basic facts required for predicting the extent of their use on the market and the risk of uncontrolled release during use. This information can be extremely valuable in selecting compounds to focus upon in suspect identification efforts, based on the chances of them being present in the environment, and in finding new pollutants that are currently off the radar of environmental chemists. Most of these data are handled as confidential business information and cannot be found in the open literature. However, in Sweden, the Chemicals Agency (KemI) has transformed the confidential data through aggregation and categorization of information into general exposure indices for different target groups. These exposure index tables were created in 2005 and have thereafter been updated annually. Nowadays, they are among others used for regulatory prioritization of selecting chemicals for national monitoring programs.

In this study, we tested the hypothesis that regulatory databases are a powerful tool for prioritization of chemical substances and increase the chances of identifying emerging environmental pollutants, i.e., chemicals of environmental concern that have so far received little or no attention. The aim of the study was to use the latest advances in HRMS and the information contained in regulatory databases to detect and identify emerging pollutants in effluents from wastewater treatment plants (WWTPs). Our intention was to help create a broader picture of the presence of emerging pollutants in the environment.

MATERIALS AND METHODS

Chemicals, Sampling, And Analysis. To characterize the wastewater in terms of well-known micropollutants, 74 substances were analyzed including pharmaceuticals and personal care products (PPCPs), per- and polyfluoroalkyl substances (PFASs), pesticides, and artificial sweeteners. At a later stage, an additional 27 substances were purchased and analyzed in order to confirm the preliminary suspect identifications. Full details about all chemicals analyzed are given in the [Supporting Information](#) (SI).

Effluent samples were taken from three large-scale WWTPs located in Sweden: Uppsala (172000 population equivalents (PE)), Stockholm (780000 PE), and Västerås (120000 PE), together covering >10% of the wastewater generated by the Swedish population. The wastewater treatment steps at these plants include mechanical treatment and primary sedimentation, biological treatment using activated sewage sludge with nitrogen removal, chemical treatment by addition of iron chloride, and lamella sedimentation to remove particulate matter. The selected WWTPs receive wastewater from both domestic and industrial settings and were representative examples for our purposes, i.e., to test whether regulatory databases can assist in prioritization of environmentally relevant substances. Twenty-four hour composite samples of effluent were collected in February 2017 in precleaned high-density polyethylene (HDPE) bottles. All samples were filtered through

glass fiber filters (pore size 0.7 μm) and stored in darkness at $-18\text{ }^{\circ}\text{C}$ until analysis.

Sample extraction was carried out in quintuplicate using the protocol previously described by Gago-Ferrero et al.¹¹ In brief, solid-phase extraction (SPE) was conducted for 200 mL of sample using four different SPE materials simultaneously (Oasis HLB, Isolute ENV+, Strata-X-AW, and Strata-X-CV) in an in-house cartridge to achieve sufficient enrichment for a broad range of compounds. To perform the screening, samples were further analyzed using an ultrahigh performance liquid chromatography (UHPLC) system coupled to a quadrupole-time-of-flight (QTOF) mass spectrometer (UHPLC-HRMS, G2S Xevo, Waters) (for details, see the SI). Quality assurance and quality control information is provided in SI.

Targeted analysis of the 74 micropollutants ([Table SI-1](#)) was carried out following the validated method previously described by Gago-Ferrero et al.⁴¹ The suspect screening was performed as outlined below. Details about the quality assurance and quality control can be found in the [Supporting Information](#) and elsewhere.⁴¹

Prioritization Based on Regulatory Database. The National Swedish Product Register (supervised by the Swedish Chemical Agency (KemI)) was used to prioritize chemicals. This register database contains information on all chemical products released on the Swedish market at volumes of at least 100 kg per year per manufacturer or importer. End products of foodstuffs, cosmetics, medicines, and hygiene products are not included in the register. However, the raw materials for these have to be registered if they occur on the Swedish market. The database contains data reported since 1992 and comprises ~23000 chemicals, of which around 14000 are present in active products (2015). Use of a consistent suspect screening approach for such an extensive list of substances is not feasible because only some parts of the data evaluation process can be completely automatized, while others need to be carefully revised by experts in order to communicate the identifications with an acceptable level of confidence, e.g., final evaluation of the MS/MS spectra.⁴ Therefore, smart prioritization is required in order to reduce the number of suspects with a high chance of being present.

As discussed previously, most information listed in national registers is confidential. However, aggregation and categorization of the original data can in many cases transform them into nonconfidential (but still useful) information. One example is the Exposure Index (EI)⁴² developed by KemI. EI values are calculated for all substances in the database that are in use in Sweden. The EI is an indicator for the possibility of a substance to expose a primary recipient, based on the total use pattern of the chemical in Sweden, while the environmental fate of the substance is not considered. Each chemical is allocated a single value between 0 (low) and 7 (high) that considers product tonnages, occurrence on the market, and dispersion to specific recipients of the chemical from end-products (e.g., goods and materials) that occurs during usage. The EI thus reflects the use and emission pattern and is recipient-specific (has different indices for, e.g., soil, air, surface water, sewage water). The calculation of the EI is done in several steps. First, a product specific exposure index (EI_{prod}) is calculated for each specific chemical in each product in the register database.⁴² EI_{prod} describes the general potential for a substance to be released from a specific product use and for its calculation the following data are used: (i) the function of the product; (ii) the product specific sector of use; and (iii) the annual tonnage of the

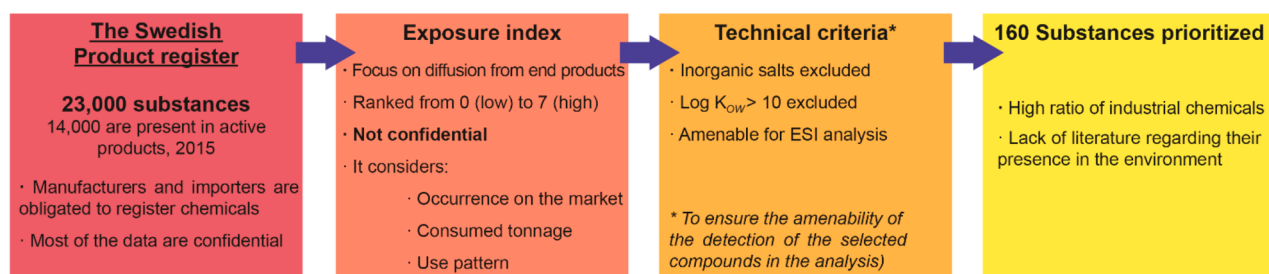


Figure 1. Prioritization workflow for creation of our suspect screening list.

substance in the product. The registrant has to select predefined functions and the sector of use. Each function and sector of use have a predefined exposure estimation, based on expert judgments.⁴³ All EI_{prod} for a substance are then added together (quantity weighted) into an overall “Exposure Index” (normalized into a scale of 0–7).

As the objective of this study was to analyze WWTP effluent, we focused solely on compounds with $EI_{sewage-water}$ values > 5 . Inorganic salts were also excluded, as were substances with $\log K_{OW} > 10$ to ensure the amenability in LC–HRMS detection and to exclude extremely hydrophobic chemicals that are readily removed in WWTPs (by sedimentation and flocculation). Other works have considered chemicals with $\log K_{OW}$ values ≤ 5 to be relevant water pollutants.⁴⁴ We opted for a higher $\log K_{OW}$ threshold since (i) approximately one-third of substances in the database with an $EI_{sewage-water}$ value between 5 and 7 had a $\log K_{OW}$ between 5 and 10, (ii) it has been demonstrated that treatments applied in conventional WWTPs lead to the release of substances with $\log K_{OW} > 5$,^{11,19} and (iii) several compounds with $\log K_{OW}$ between 5 and 10 have previously been detected in WWTP effluent samples.^{11,45} In a last step, compounds that were not ionizable with electrospray in LC–HRMS analysis (based on expert knowledge) were also excluded. Finally, of the initial 23000 compounds, 160 were selected as suspects (Figure 1, Table SI-2). The hypothesis tested was that these substances have a high possibility of being present in wastewater, although for most there is a lack of information in the literature on their occurrence in the aquatic environment.

Suspect-Screening Performance. Tentative identification of the suspects was carried out following the workflow previously described by Gago-Ferrero et al.¹¹ In brief, the criteria used for reduction of features in both ionization modes (ESI(+)) and ESI(–)) include (i) a threshold in peak area (≥ 200 for ESI(+)) and ≥ 100 for ESI(–)), (ii) a threshold in intensity counts (≥ 100 for ESI(+)) and ≥ 50 for ESI(–)), which is roughly equivalent to a signal-to-noise ratio of 10), (iii) a threshold in mass accuracy of ± 2 mDa on the monoisotopic peaks, (iv) a good isotopic pattern fit, and (v) chromatographic retention time (Rt) plausibility using a quantitative structure-retention relationships (QSRR) prediction model.⁴⁶ Additional evidence to support the identifications was obtained based on in-depth scrutiny of the MS/MS spectra by comparison with spectral libraries (European MassBank)⁴⁷ using in silico fragmentation software (MetFrag⁴⁸ and CFM-ID⁴⁹) and expert knowledge. For tentatively identified substances that were commercially available, the reference substances were purchased in order to confirm the identity. The concentrations of the confirmed compounds in the samples (semiquantitative analysis) were determined by standard addition (by considering the recoveries calculated afterward).

The level of confidence in identification of the detected compounds was communicated according to the system described by Schymanski et al.,⁵⁰ where level 1 corresponds to confirmed structures (with reference standard), level 2a to probable structures by library spectrum match, level 2b to probable structures by diagnostic evidence, level 3 to tentative candidate(s), level 4 to unequivocal molecular formulas, and level 5 to exact mass(es) of interest.

RESULTS AND DISCUSSION

Characterization of Effluent Samples in Terms of Well-Known Micropollutants. In total, 58 of the 74 target substances were detected at least once, and 47 compounds were detected in all samples, demonstrating the ubiquitous presence of xenobiotics (Table SI-3). Some compounds were found at particularly high concentrations, including metoprolol (up to 1800 ng L⁻¹), metformin (up to 1400 ng L⁻¹), losartan (up to 670 ng L⁻¹), tramadol (up to 510 ng L⁻¹), furosemide (up to 470 ng L⁻¹), caffeine (up to 410 ng L⁻¹), atenolol (up to 370 ng L⁻¹), and diclofenac (up to 290 ng L⁻¹), among others. These levels are within the range reported in previous studies that analyzed treated wastewater in the study region^{51,52} and also in other regions of Europe.⁵³ Therefore, the samples analyzed in this study were representative WWTP effluent samples to test the hypothesis that regulatory databases can be an efficient tool for prioritizing compounds that are little studied but have a high chance of being discharged to the environment.

Identification of the Prioritized Suspects. Screening for the prioritized chemicals (the suspects) in the effluent samples at the selected locations yielded 27 hits using ESI(+) and 46 using ESI(–) mode when applying the previously described thresholds of ion intensity, peak area, mass accuracy, isotopic fit, and chromatographic Rt (see Materials and Methods). There was an overlap of 10 compounds detected in both modes. The Rt prediction model reduced the number of hits by 25%, showing that the use of a reliable Rt prediction model increases the chances of high accuracy and saves time and effort.

Since a multitude of compounds (from one to several thousands) can share a given molecular formula, additional investigations of the MS/MS spectra (using available spectral libraries (MassBank) and in silico fragmentation prediction tools (MetFrag) were performed in order to reach tentative identifications.⁴ For compounds at level 4 (unequivocal molecular formula) or 5 (exact mass of interest) for which no additional evidence could be found (Table SI-4), no further investigation was conducted within this study. Following this workflow, the 73 hits were reduced to 40 tentatively identified compounds (levels 2 and 3). In the last step, available reference standards were purchased. After comparing Rt and MS/MS

Table 1. Details on the 36 Tentatively Identified and Confirmed Suspect Analytes Including Additional Evidence That Leads to Their Identification, Information Related to Their Consumption and Use, and Semiquantitative Values (for Confirmed Compounds)



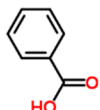
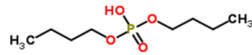
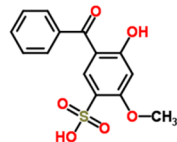
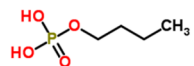
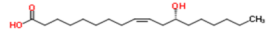
Suspect analyte	Rt ^a (min)	Additional Evidences for the identification	Product quantity ^b	Type of products/ industrial category ^b	Level of confidence ^c	Conc. range [ng/L] (n = 3)
Sebacic acid 	0.78	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 99.0445 [C₃H₇O₂]; 109.0655 [C₇H₉O]; 165.0916 [C₁₀H₁₃O₂] Similarity with MassBank [record PR100605] CONFIRMED with ref. standard 	287 tonnes 116 products	<ul style="list-style-type: none"> Antifreeze Coolants and lubricants for metal shearing and metal forming Grinding fluids Heat transferring agents Maintenance and repair garages for motor vehicles Sale, maintenance and repair for motor vehicles Industry for fabricated metal products Electricity, gas, steam and air conditioning supply 	1	57-110
C₁₀H₁₈O₄ [M-H]⁻ Acesulfame 	0.83	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 82.0293 [C₄H₄NO] Similarity with MassBank [record EA275659] CONFIRMED with ref. standard 	16 tonnes 6 products	<ul style="list-style-type: none"> Food additive Sweetener Food industry 	1	1200-16000
C₇H₅NO₄S [M-H]⁻ Benzoic acid 	0.87	<ul style="list-style-type: none"> Presence of the fragment <i>m/z</i>: 77.0397 [C₆H₅] CONFIRMED with ref. standard 	33 tonnes 186 products	<ul style="list-style-type: none"> In-car preservatives Binders for paints, adhesives Stabilizers Biocides for human hygiene Perfumes and toiletries Paint industry Industry for cleaning and polishing preparations Industry for pulp, paper and paper products Maintenance and repair garages for motor vehicles 	1	550-1300
C₇H₆O₂ [M-H]⁻ Dibutyl phosphate 	4.38	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 78.9583 [O₃P]; 96.9691 [H₂O₄P]; 153.0317 [C₄H₁₀O₄P] CONFIRMED with ref. standard 	1 tonne 49 products	<ul style="list-style-type: none"> Sealant Brake fluid Export Industry for cleaning and polishing preparations Sales establishment for motor vehicle parts and accessories Construction of buildings 	1	76-370
C₈H₁₉O₄P [M-H]⁻ Sulisobenzene 	4.63	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9568 [O₃S]; 210.0321 [C₁₃H₆O₃]; 228.9809 [C₈H₅O₆S] Similarity with MassBank [record TUE00147] CONFIRMED with ref. standard 	0.4 tonnes 21 products	<ul style="list-style-type: none"> Raw material for cosmetics and hygienic articles Washing-up liquids Retail sale, except for such with motor vehicles 	1	120-1100
C₁₄H₁₂O₆S [M-H]⁻ Mono-n-butylphosphoric acid 	4.76	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 78.9583 [O₃P]; 96.9691 [H₂O₄P]; 137.0004 [C₃H₆O₄P] CONFIRMED with ref. standard 	1 tonne 52 products	<ul style="list-style-type: none"> Brake fluid Export Industry for cleaning and polishing preparations Sales establishment for motor vehicle parts and accessories 	1	72-250
C₈H₁₁O₄P [M-H]⁻ Ricinoleic acid 	8.70	<ul style="list-style-type: none"> Presence of characteristic fragment <i>m/z</i>: 279.2324 [C₁₈H₃₁O₂]; 183.1385 [C₁₁H₁₉O₂] CONFIRMED with ref. standard 	0.8 tonnes 5 products	<ul style="list-style-type: none"> Coolants and lubricants for metal handling 	1	2600-6600
C₁₈H₃₄O₃ [M-H]⁻						

Table 1. continued

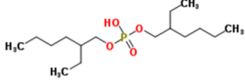
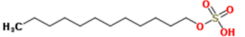
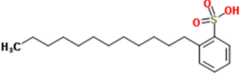
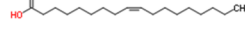
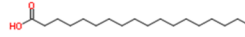
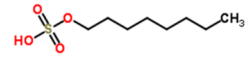
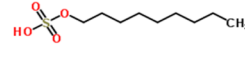
Suspect analyte	Rt ^a (min)	Additional Evidences for the identification	Product quantity ^b	Type of products/ industrial category ^b	Level of confidence ^c	Conc. range [ng/L] (n = 3)
Di-(2-ethylhexyl)phosphoric acid  $C_{16}H_{35}O_4P$ [M-H] ⁻	9.38	<ul style="list-style-type: none"> Presence of characteristic fragments m/z: 78.9584 [O₃P]; 123.9923 [C₂H₅O₄P]; 209.0945 [C₈H₁₈O₄P] CONFIRMED with ref. standard 	2.2 tonnes 58 products	<ul style="list-style-type: none"> Gear oil Lubricant additives Industry for machinery and equipment Export Surface treatment and coating for metals Industry for motor vehicles Industry for coke, refined petroleum products 	1	14-150
Laurilsulfate (C12-AS)  $C_{12}H_{26}O_4S$ [M-H] ⁻	9.27	<ul style="list-style-type: none"> Presence of characteristic fragments m/z: 79.9567 [O₃S]; 96.9688 [HO₄S]; 136.9905 [C₃H₅O₄S] CONFIRMED with ref. standard 	0.3 tonnes 6 products	<ul style="list-style-type: none"> Cleaning products 	1	660-1800
2-Dodecylbenzenesulfonic acid  $C_{18}H_{30}O_3S$ [M-H] ⁻	10.77/ 10.9	<ul style="list-style-type: none"> Presence of characteristic fragments m/z: 183.01196 [C₈H₇O₃S]; 198.0357 [C₉H₁₀O₃S]; 79.9560 [O₃S]; 170.0037 [C₇H₆O₃S]; 197.0271 [C₉H₉O₃S] Plausible MS/MS spectra also in PI Plausible Rt in PI (12.49) according to the QSRR model CONFIRMED with ref. standard 	88 tonnes 147 products	<ul style="list-style-type: none"> Car shampoo Paint, other solvent based for industry use Catalysts Cleaner Foam cleaner Production of other chemical products but synthetic fibres Export Sale, maintenance and repair of motor vehicles Surface treatment and coating of metals Paint industry 	1	5800-22000
Oleic acid  $C_{18}H_{34}O_2$ [M-H] ⁻	12.51	<ul style="list-style-type: none"> Presence of characteristic fragment m/z: 263.2379 [C₁₈H₃₁O] CONFIRMED with ref. standard Similarity with MassBank [record MT000029] 	160 tonnes 309 products	<ul style="list-style-type: none"> Surface active agents Detergents Lubricant additives Coolants and lubricants for metal shearing Paint industry Surface treatment and coating of metals Production of other chemical products but synthetic fibres Publishers and printers Export 	1	210-600
Stearic acid  $C_{18}H_{36}O_2$ [M-H] ⁻	12.53	<ul style="list-style-type: none"> Presence of characteristic fragments m/z: 83.0494 [C₈H₇O]; 255.2317 [C₁₆H₃₁O₂]; 265.2535 [C₁₈H₃₃O] Similarity with MassBank [record MT000015] CONFIRMED with ref. standard 	6660 tonnes 282 products	<ul style="list-style-type: none"> Raw material, intermediates that are not mentioned elsewhere Raw material for cosmetics and hygienic articles Material insulating from electricity Lubricants Putty Export Industry for pulp, paper and paper products Industry for organic basic chemicals Production of other chemical products but synthetic fibres Industry for plastic and rubber products 	1	41000-230000
Octyl hydrogen sulfate (C8-AS)  $C_8H_{18}O_4S$ [M-H] ⁻	6.08	<ul style="list-style-type: none"> Presence of characteristic fragments m/z: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	33 tonnes 3 products	<ul style="list-style-type: none"> Surfactant in fire-fighting foam Cleaning products 	3	
Nonyl hydrogen sulfate (C9-AS)  $C_9H_{20}O_4S$ [M-H] ⁻	6.90	<ul style="list-style-type: none"> Presence of characteristic fragments m/z: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	33 tonnes 3 products	<ul style="list-style-type: none"> Surfactant in fire-fighting foam Cleaning products 	3	

Table 1. continued

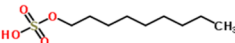
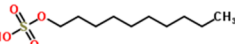
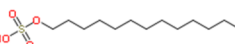
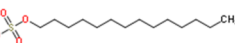
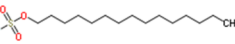
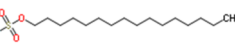
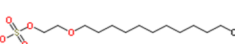
Suspect analyte	Rt ^a (min)	Additional Evidences for the identification	Product quantity ^b	Type of products/ industrial category ^b	Level of confidence ^c	Conc. range [ng/L] (n = 3)
Nonyl hydrogen sulfate (C9-AS) 	6.90	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	33 tonnes 3 products	<ul style="list-style-type: none"> Surfactant in fire-fighting foam Cleaning products 	3	
C ₉ H ₂₀ O ₄ S [M-H] ⁻						
Decyl hydrogen sulfate (C10-AS) 	7.60	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	33 tonnes 3 products	<ul style="list-style-type: none"> Surfactant in fire-fighting foam Cleaning products 	3	
C ₁₀ H ₂₂ O ₄ S [M-H] ⁻						
Tridecyl hydrogen sulfate (C13-AS) 	9.94	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	2.2 tonnes 5 products	<ul style="list-style-type: none"> Cleaning/washing agent for dish washing 	3	
C ₁₃ H ₂₈ O ₄ S [M-H] ⁻						
Tetradecyl hydrogen sulfate (C14-AS) 	10.9	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	2.2 tonnes 5 products	<ul style="list-style-type: none"> Cleaning/washing agent for dish washing 	3	
C ₁₄ H ₃₀ O ₄ S [M-H] ⁻						
Pentadecyl hydrogen sulfate (C15-AS) 	11.7	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	2.2 tonnes 5 products	<ul style="list-style-type: none"> Cleaning/washing agent for dish washing 	3	
C ₁₅ H ₃₂ O ₄ S [M-H] ⁻						
Hexadecyl hydrogen sulfate (C16-AS) 	12.16	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9599 [O₃S]; 96.9596 [HO₄S] Best match with MetFrag RT is consistent among the analogue series RT and MSMS spectra plausible with the confirm compound Laurilsulfate 	2.2 tonnes 5 products	<ul style="list-style-type: none"> Cleaning/washing 	3	
C ₁₆ H ₃₄ O ₄ S [M-H] ⁻						
2-(Dodecyloxy)ethyl hydrogen sulfate (C12-AE1S) 	10.33	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9568 [O₃S]; 95.9517 [O₄S]; 96.9590 [HO₄S]; 122.9752 [C₂H₃O₄S]; 138.9701 [C₂H₃O₂S]; 183.1749 [C₁₂H₂₃O] Similarity with MassBank [record ETS00008] RT is consistent among the analogue series Good match with MetFrag 	32 tonnes 16 products	<ul style="list-style-type: none"> Raw material for cosmetics 	2a	
C ₁₄ H ₃₀ O ₅ S [M-H] ⁻						

Table 1. continued

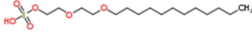
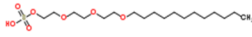
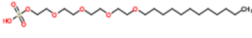
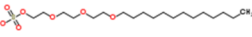
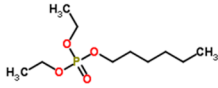
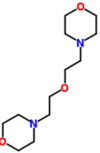
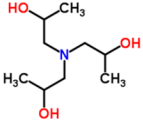
Suspect analyte	Rt ^a (min)	Additional Evidences for the identification	Product quantity ^b	Type of products/ industrial category ^b	Level of confidence ^c	Conc. range [ng/L] (n = 3)
2-[2-(Dodecyloxy)ethoxy]ethyl hydrogen sulfate (C12-AE2S)	10.68	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9568 [O₃S]; 95.9517 [O₄S]; 96.9590 [HO₄S], 122.9752 [C₂H₃O₄S]; 167.0019 [C₄H₇O₂S]; 183.1749 [C₁₂H₂₃O] RT is consistent among the analogue series Best match in MetFrag 	32 tonnes 16 products	<ul style="list-style-type: none"> Raw material for cosmetics 	2b	
 C ₁₆ H ₃₄ O ₆ S [M-H] ⁻						
2-[2-[2-(Dodecyloxy)ethoxy]ethoxy]ethyl hydrogen sulfate (C12-A-3S)	10.72	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9568 [O₃S]; 95.9517 [O₄S]; 96.9590 [HO₄S]; 122.9752 [C₂H₃O₄S]; 167.0019 [C₄H₇O₂S]; 211.0276 [C₆H₁₁O₆S] RT is consistent among the analogue series Best match in MetFrag 	32 tonnes 16 products	<ul style="list-style-type: none"> Raw material for cosmetics 	2b	
 C ₁₈ H ₃₈ O ₇ S [M-H] ⁻						
3,6,9,12-Tetraoxatetradecan-1-yl hydrogen sulfate (C12-AE4S)	11.05	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9568 [O₃S]; 95.9517 [O₄S]; 96.9590 [HO₄S]; 122.9752 [C₂H₃O₄S]; 167.0019 [C₄H₇O₂S]; 183.1749 [C₁₂H₂₃O]; 211.0276 [C₆H₁₁O₆S]; 255.2329 [C₁₆H₃₁O₂] RT is consistent among the analogue series Best match in MetFrag 	32 tonnes 16 products	<ul style="list-style-type: none"> Raw material for cosmetics 	2b	
 C ₂₀ H ₄₂ O ₈ S [M-H] ⁻						
2-[2-[2-(Tridecyloxy)ethoxy]ethoxy]ethyl hydrogen sulfate (C13-AE3S)	11.3	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 79.9568 [O₃S]; 96.9590 [HO₄S]; 122.9752 [C₂H₃O₄S]; 269.2485 [C₁₇H₃₃O₂] Best match in MetFrag 	9.9 tonnes 47 products	<ul style="list-style-type: none"> Raw material for cosmetics 	3	
 C ₁₉ H ₄₀ O ₇ S [M-H] ⁻						
Diethyl hexyl phosphate	10.95	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 78.9583 [O₃P]; 96.9691 [H₂O₄P]; 209.0943 [C₈H₁₈O₄P] 	2.5 tonnes 20 products	<ul style="list-style-type: none"> Gear oil Sale, maintenance and repair of motor vehicles 	3	
 C ₁₀ H ₂₃ O ₄ P [M-H] ⁻						
2,2'-Dimorpholinyl-diethyl-ether	0.82	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 114.0919 [C₆H₁₂NO]; 86.0964 [C₅H₁₂N]; 158.1181 [C₈H₁₆NO₂]; 112.0757 [C₆H₁₀NO]; 70.0651 [C₄H₈N]; 84.0801 [C₅H₁₀N] CONFIRMED with ref. standard 	4.9 tonnes 102 products	<ul style="list-style-type: none"> Sealant Putty Adhesives, solvent based for industrial use Catalysts Insulating materials, heat-cold Construction of buildings Export Civil engineering Retail sale, except for such with motor vehicles Industry for wood and products of wood 	1	14-24
 C ₁₂ H ₂₄ N ₂ O ₃ [M+H] ⁺ , [M+Na] ⁺						
Triisopropanolamine	0.84	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 174.1488 [C₉H₂₀NO₂]; 98.0964 [C₆H₁₂N]; 156.1383 [C₉H₁₈NO]; 116.1070 [C₆H₁₄NO] CONFIRMED with ref. standard 	6 tonnes 294 products	<ul style="list-style-type: none"> Binders for paints, adhesives Paint, solvent based with anti-corrosive effect for other use Paint, other water based for industrial use Export Paint industry Industry for pulp, paper and paper products Sale, maintenance and repair of motor vehicles Sales establishment for motor vehicle parts and accessories 	1	6-21
 C ₉ H ₂₁ NO ₃ [M+H] ⁺ , [M+Na] ⁺						

Table 1. continued

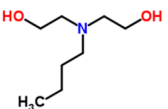
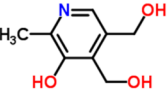
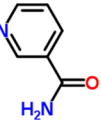
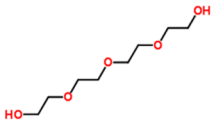
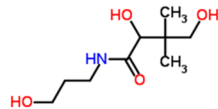
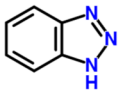
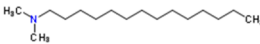
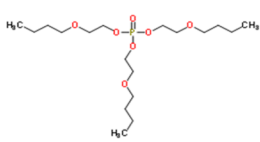
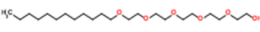
Suspect analyte	Rt ^a (min)	Additional Evidences for the identification	Product quantity ^b	Type of products/ industrial category ^b	Level of confidence ^c	Conc. range [ng/L] (n = 3)
N-Butyl-diethanolamine 	0.86	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 144.1388 [C₈H₁₉NO]; 88.0762 [C₄H₁₀NO]; 106.0868 [C₄H₁₂NO₂]; 100.1126 [C₆H₁₄N] CONFIRMED with ref. standard 	36 tonnes 10 products	<ul style="list-style-type: none"> Metalworking and functional fluids (e.g. brake fluid) 	1	21-78
C ₈ H ₁₉ NO ₂ [M+H] ⁺ , [M+Na] ⁺						
Pyridoxine 	1.01	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 134.0600 [C₈H₉NO]; 152.0706 [C₈H₁₀NO₂]; 124.0757 [C₇H₁₀NO]; 106.0651 [C₇H₈N] Similarity with MassBank [record KO003754] CONFIRMED with ref. standard 	Not available	<ul style="list-style-type: none"> Food additive in beverage, veterinary and pharmaceutical industry 	1	5-53
C ₈ H ₁₁ NO ₃ [M+H] ⁺						
Nicotinamide 	1.05	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 80.0495 [C₅H₆N]; 108.0444 [C₆H₈NO]; 106.0287 [C₆H₈NO] CONFIRMED with ref. standard 	0.4 tonnes 7 products	<ul style="list-style-type: none"> Raw material for cosmetics and hygienic articles Food and fodder additives 	1	32-91
C ₆ H ₆ N ₂ O [M+H] ⁺						
Tetraethyleneglycol 	1.72 (-0.89)	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 133.0855 [C₈H₁₃O₃]; 89.0594 [C₄H₉O₂]; 103.0387 [C₄H₇O₃] CONFIRMED with ref. standard 	264 tonnes 110 products	<ul style="list-style-type: none"> Hardener Joint-less floors Curing agent for plastics Filling, filler Paint, other curing paint for industrial use Export Paint industry Surface treatment and coating of metals Specialized construction activities Construction of buildings 	1	1500-3300
C ₈ H ₂₃ N ₅ [M+H] ⁺ , [M+Na] ⁺ , [M+NH ₄] ⁺						
Panthenol 	1.75	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 188.1281 [C₉H₁₈NO₃]; 76.0757 [C₃H₁₀NO]; 170.1176 [C₉H₁₆NO₂]; 102.0549 [C₄H₈NO₂]; 103.0754 [C₅H₁₁O₂] Similarity with MassBank [record BML01113] CONFIRMED with ref. standard 	16 tonnes 43 products	<ul style="list-style-type: none"> Vitamins Raw material for cosmetics and hygienic articles Biocides for human hygiene Veterinary pharmaceuticals Industry for perfumes and toiletries Wholesale trade Retail sale, except for such with motor vehicles Agriculture 	1	41-340
C ₉ H ₁₉ NO ₄ [M+H] ⁺ , [M+Na] ⁺ , [M+NH ₄] ⁺						
1,2,3-Benzotriazole 	3.82	<ul style="list-style-type: none"> Presence of the fragment <i>m/z</i>: 92.0494 [C₆H₆N] Plausible MS/MS spectra also in NI Plausible Rt also in NI (1.88) according to the QSRR model Similarity with MassBank [record AU405003] CONFIRMED with ref. standard 	23 tonnes 353 products	<ul style="list-style-type: none"> Coolants and lubricants for metal processing and metal shearing Antifreeze Corrosion inhibitors Retail sale, except for such with motor vehicles Industry for fabricated metal products Industry for pulp, paper and paper products Export Industry for motor vehicles 	1	160-760
C ₆ H ₅ N ₃ [M+H] ⁺						
N,N-Dimethyl-1-tetradecanamine 	12.01	<ul style="list-style-type: none"> Presence of characteristic fragments <i>m/z</i>: 228.2691 [C₁₅H₃₄N]; 214.2529 [C₁₄H₃₂N]; 85.1012 [C₆H₁₃] CONFIRMED with ref. standard 	2.4 tonnes 13 products	<ul style="list-style-type: none"> Cleaner Impregnation agents for textile Manufacture of textiles 	1	12-72
C ₁₆ H ₃₅ N [M+H] ⁺						

Table 1. continued

Suspect analyte	Rt ^a (min)	Additional Evidences for the identification	Product quantity ^b	Type of products/ industrial category ^b	Level of confidence ^c	Conc. range [ng/L] (n = 3)
Tris(2-butoxyethyl) phosphate 	12.87 (13.64)	<ul style="list-style-type: none"> ▪ Presence of characteristic fragments m/z: 98.9837 [H_4O_4P]; 143.0096 [$C_2H_8O_5P$]; 199.0714 [$C_6H_{16}O_5P$]; 299.1607 [$C_{12}H_{28}O_6P$] ▪ Similarity with MassBank [record SM880602] ▪ CONFIRMED with ref. standard 	19 tonnes 180 products	<ul style="list-style-type: none"> • Waxes and other floor polishes • Polish • Paint, other water based for industrial use • Cleaner • Paint, other water based for interior use <hr/> <ul style="list-style-type: none"> • Cleaning companies and chimney-sweepers • Export • Paint industry • Wholesale of chemical products • Manufacture of textiles 	1	17-2200
$C_{18}H_{39}O_7P$ [M+H] ⁺ , [M+Na] ⁺ Pentaethylene glycol monododecyl ether / Laureth 5 	14.24	<ul style="list-style-type: none"> ▪ Presence of characteristic fragments m/z: 133.0859 [$C_6H_{13}O_3$]; 89.0597 [$C_4H_9O_2$]; 177.1121 [$C_8H_{17}O_4$]; 239.1489 [$C_{10}H_{23}O_6$]; 221.1383 [$C_{10}H_{21}O_5$]; 257.2475 [$C_{16}H_{33}O_2$] ▪ CONFIRMED with ref. standard 	< 10 tonnes 1 product	<ul style="list-style-type: none"> • Raw material for cosmetics and hygienic articles 	1	14-42
$C_{22}H_{46}O_6$ [M+H] ⁺ , [M+Na] ⁺ , [M+NH ₄] ⁺						

^aRt = retention time ; Conc. = concentration ; ref standard = reference standard. ^bNational Swedish Product Register. ^cLevels of confidence: 1 = confirmed structure, 2a = probable structure by library, 2b = probable structure by diagnostic evidence, 3 = tentative candidate, 4 = unequivocal molecular formula, 5 = mass of interest.

spectra with the reference compounds, four more compounds were rejected (benzylamine, dazomet, diethyl thiourea, and natamycin). Table 1 summarizes the 36 compounds confirmed with standard ($n = 23$) or tentatively identified ($n = 13$) with their corresponding level of confidence, Rt, detected adducts, the additional evidence that led to their identification, and information related to their consumption, their area of application, and semiquantitative values obtained for the confirmed compounds. In addition, the MS/MS spectra have been included in the SI (Figure SI-2) for compounds for which this information is not available in Massbank.

The identification methodology can be exemplified for the case of 2,2-dimorpholinyl-diethyl ether (Figure 2). The chromatographic peak associated with this substance met all threshold conditions applied in the feature reduction steps, including a plausible Rt according to the QSRR model.⁴⁶ These facts made this suspect a suitable candidate for further investigation. MS/MS spectra for this substance were not found in the MassBank spectral database. However, the fragments at m/z 158.118, 114.0919, 112.0757, 86.0964, 84.0801, and 70.0651 fit very well with the investigated substance, corresponding to [$C_8H_{16}NO_2$], [$C_6H_{12}NO$], [$C_6H_{10}NO$], [$C_5H_{12}N$], [$C_5H_{10}N$], and [C_4H_8N], respectively. It also provided the highest MetFrag score using the Chemspider database. Therefore, this substance was considered tentatively identified at level 2b (and would have remained at this level if the corresponding standard was not available). However, the reference standard was purchased, and the identification was confirmed by MS/MS and Rt comparison, reaching level 1. The concentrations in the samples analyzed were in the range 14–24 ng L⁻¹. The compound 2,2-dimorpholinyl-diethyl ether is used as sealant and adhesive, mainly in industry and, to the best of our knowledge, has not been detected previously in water samples.

It was possible to use data from the spectral library MassBank in several cases, increasing the confidence in the identifications.

One such case was tris(2-butoxyethyl) phosphate, summarized in Figure S1. The fragments at m/z 98.9837, 199.0714 and 299.1607 are characteristic for that substance, corresponding to [H_4O_4P], [$C_6H_{16}O_5P$], and [$C_{12}H_{28}O_6P$], respectively. They fit very well with the MassBank spectrum record SM880602, leading to level 2a identification. Finally, this compound was confirmed with a reference standard. MassBank was also used in the identification of sebacic acid, 1,2,3-benzotriazole, sulisobenzone, stearic acid, 2-(dodecyloxy)ethyl hydrogen sulfate, acesulfame, pyridoxine, and panthenol.

In other cases, finding a plausible Rt between different substances belonging to a given homologous series was also used as additional evidence. This was the case for alkyl sulfates (AS). Laurilsulfate (C12-AS) was confirmed with a reference standard. For the rest of the ASs (C8-AS–C16-AS), it was observed that their Rt increased constantly with number of carbons, and the MS/MS spectra showed the same characteristic fragments (m/z 79.9568 [O_3S] and 96.9596 [HO_4S]). Those AS compounds were tentatively identified at level 3; although evidence for a possible structure exists, there is insufficient information for the exact structure (i.e., positional isomers). A similar observation was made for the series of alkyl ethoxy sulfates (AES), where C12-AE1S was tentatively identified at level 2a and C12-AE2S, C12-AE3S, C12-AE4S, and C13-AE3S at level 3.

In total, of the 160 prioritized compounds, 40 were tentatively identified and 23 were finally confirmed with a reference standard. Only four compounds were rejected on checking their identity against the reference standard, which demonstrates the suitability of the suspect screening approach and the prioritization strategy (see the following sections) for our purposes.

Environmental Relevance of the Identified Suspects. Nonconfidential industrial category and number and type of products in which each identified compound has applications, along with the respective annual production volume and

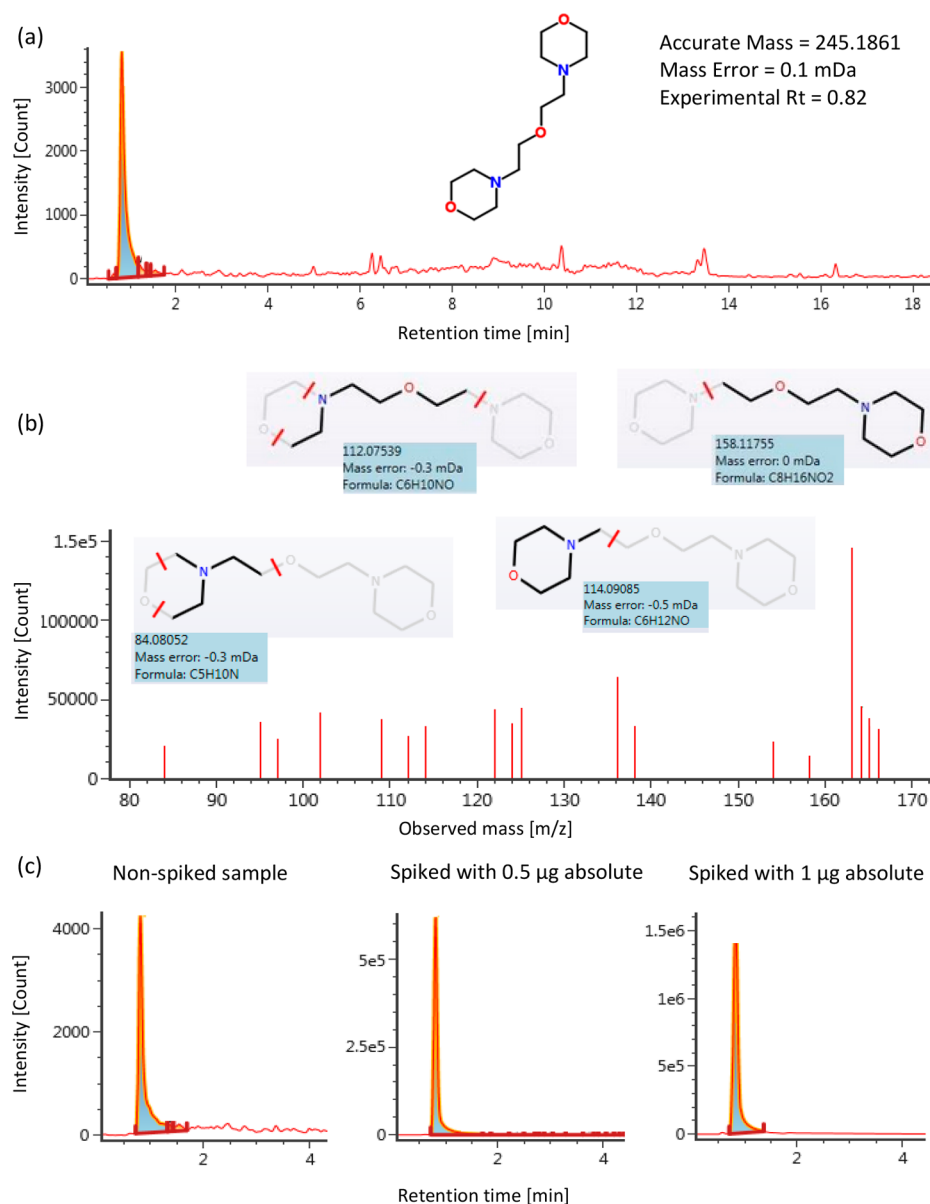


Figure 2. Identification of the compound 2,2-dimorpholinylethyl ether: (a) full MS chromatogram for the corresponding mass (± 2.5 mDa); (b) MS/MS spectra and corresponding fragments; (c) confirmation step using standard addition.

concentration ranges (semiquantitative data), are summarized in Table 1. In addition, toxicity values for the tentatively identified and confirmed suspect compounds were estimated, based on the ecological structure–activity relationships (ECOSAR) predictive model (Table SI-5).⁵⁴ Recipient, reference unit, threshold levels, and levels of concern are summarized for tentatively identified and confirmed compounds

A few of the identified compounds are widely described in the literature as common micropollutants. These include the artificial sweetener acesulfame, the food preservative benzoic acid, the UV filter sulisobenzone, and the corrosion inhibitor 1,2,3-benzotriazole. Acesulfame showed some of the highest concentrations of all confirmed compounds, reaching levels above 15000 ng L⁻¹. This is in agreement with previous findings that acesulfame is one of the most abundant substances in wastewater and surface water due to its high consumption in urban areas.¹¹ Sulisobenzone, benzoic acid, and 1,2,3-

benzotriazole exhibited equally high levels, reaching concentrations above 1000 ng L⁻¹, which is comparable to the level reported in other studies. The aquatic toxicity according to the ECOSAR prediction model was moderate (i.e., acesulfame, benzoic acid) to high (i.e., 1,2,3-benzotriazole, sulisobenzone). The endocrine disruptive effects described for sulisobenzone⁵⁵ and its widespread occurrence in surface waters^{11,56,57} make it a candidate for inclusion in monitoring programs.

Several sulfonate anionic surfactants were identified. Regarding the AS, compounds between C8-AS and C16-AS were detected and the confirmed substance laurilsulfate (C12-AS) occurred in concentrations ranging from 660 to 1800 ng L⁻¹. The other AS could not be confirmed due to lack of commercial standards, but their chromatographic peak intensity was equal to or higher than that of C12-AS, suggesting a similar range of concentration. Alkyl sulfates are widely used in the formulation of cleaning products and are prioritized for further ecotoxicological assessment using real tests, according to

ECOSAR. These compounds can also be TPs from AES.⁵⁸ Five additional AES were tentatively identified (i.e., C12-AE1S, C12-AE2S, C12-AE3S, C12-AE4S, and C13-AE3S) showing peaks with large intensity. These surfactants are used as raw materials for cosmetics and are classified as a moderate aquatic toxicity concern. Although these substances show good removal efficiencies in WWTPs, AES are often TPs of other, more complex surfactants and release to the environment is probable, with unknown effects.⁵⁹ Far more alarming, however, is the surfactant 4-dodecylbenzenesulfonic acid (widely used in painting and cleaning products, among others), which was detected at very high levels (5800–22400 ng L⁻¹) and is estimated to be ecotoxicologically relevant.⁶⁰ Other non-sulfonated surfactants identified were tetraethylene glycol and laureth 5 (used in a variety of products related to the paint industry and cosmetics, respectively) and oleic acid, stearic acid, and sebacic acid (widely used in the manufacture of detergents, soaps, and cosmetics, or as plasticizers). These substances were confirmed in all samples. High levels were determined for all of these, but particularly for sebacic acid (41000–230000 ng L⁻¹), which exceeded the highest ever level reported in the literature for this compound in water samples. Ricinoleic acid was determined at levels up to 6500 ng L⁻¹, and to the best of our knowledge, this is the first evidence of its presence in wastewater. However, some of these substances (oleic acid, stearic acid, and sebacic acid) also show high natural occurrence and are not environmentally toxic.⁵⁴

The situation appears different for the five identified organophosphate compounds, namely di(2-ethylhexyl)-phosphoric acid, dibutyl phosphate, diethylhexyl phosphate, mono-*n*-butylphosphoric acid, and tris(2-butoxyethyl) phosphate. All of these have high predicted toxicity values, and in some cases, this toxicity has been experimentally demonstrated.^{61–66} Tris(2-butoxyethyl) phosphate is widely used in the painting industry, and it was detected at concentrations of 17–2200 ng L⁻¹, as also reported in previous studies.^{38,67,68} The other organophosphates, exclusively consisting of phosphoric acid di- and monoesters, have been less described in the literature.^{66,69–72} Concentrations of the here detected organophosphates (excluding tris(2-butoxyethyl) phosphate) were detected in the range 14–360 ng L⁻¹ and are remarkably higher than those previously reported.⁷³ This might be explained by high loads in the sewage or microbial hydrolysis of phosphoric acid triesters to the corresponding diesters.⁷³ Considering their high use, high toxicity, and high levels found in WWTP effluent (up to 750 ng L⁻¹), more attention is needed regarding the presence of these compounds, mainly used as plasticizers, in the environment.

For the first time, to the best of our knowledge, the presence of triisopropanolamine (concentration range between 6 and 21 ng L⁻¹) was reported in environmental samples. This substance is used as an emulsifier or stabilizer in various industrial applications. Other compounds whose presence was reported for the first time in environmental samples were *N*-butyldiethanolamine (21–78 ng L⁻¹) and *N,N*-dimethyl-1-tetradecanamine (12–72 ng L⁻¹), mainly used in the metal and textile industry, respectively. All three of these compounds are toxicologically relevant according to the ECOSAR model. Hence, more studies focusing on the distribution, fate, and toxicity of these chemicals are needed in order to evaluate their potential risks to the environment. Other noteworthy substances that were identified in the present study were panthenol (41–340 ng L⁻¹), pyridoxine (5–53 ng L⁻¹), and

nicotinamide (32–91 ng L⁻¹), which are used as raw materials in cosmetics and hygiene articles and as food additives.

Efficiency of the Prioritization Strategy Based on Regulatory Databases in the Selection of Suspects. The results in this study demonstrated that regulatory databases are a powerful tool in the selection of chemicals to monitor. Thirty-six compounds were identified (23 confirmed) from a suspect screening list of 160 compounds. It is noteworthy that this list included mainly uninvestigated or only partly investigated substances. These facts confirm the good performance of the prioritization approach (and the suspect screening approach).

Several prioritization approaches for organic pollutants are described in the literature, most of which compare modeled or measured occurrence concentrations and/or toxicological impacts.⁷⁴ The majority of these approaches focus on the occurrence in surface waters by assessing monitoring data^{65,75,76} and on the establishment of toxicity rankings for already known suspect compounds. This is understandable in view of the wide range of prioritization methods that have been proposed for pharmaceuticals.^{77–79} However, these strategies are biased since only substances that have previously been found in other studies are considered, which creates a loop whereby most studies focus on the same compounds. Meanwhile, a large number of potentially hazardous compounds for the environment remain hidden. As the results of the present study show, the use of market data from regulatory databases allows the range of substances of interest to be extended to include, e.g., many industrial compounds that can easily reach the environment and are rarely studied by environmental chemists.

Studies using market data for prioritization purposes are very scarce. Chiaia-Hernandez et al.³⁴ compiled a suspect list based on consumption data (including insecticides, fungicides, biocides, acaricides, pharmaceuticals, and metabolites) and confirmed the presence of three relevant substances in sediments. Other interesting studies have used national databases to screen for pesticides (and TPs) and have identified >100 pesticides and TPs, some of them for the first time, showing the good performance of those approaches.^{6,39} Another study has investigated compounds authorized on the market considering European regulatory frameworks under REACH.⁸⁰ However, only very well-known compounds could be identified (e.g., caffeine or tramadol), since MS/MS data were not considered for the identifications.

Prioritization based on the Swedish EI proved to be a good strategy in order to obtain relevant lists of compounds with a significant risk of being present in the Swedish environment. As mentioned above, of the 160 selected compounds, 36 were identified. A few of the identified compounds have been commonly detected previously in environmental studies (e.g., acesulfame or sulisobenzone).^{11,55–57} However, to the best of our authors knowledge, most identified substances have been rarely studied or not at all (e.g., 2,2'-dimorpholino-diethyl ether). This clearly shows one of the main advantages of our prioritization strategy, that the prioritization list obtained is not biased by previous studies focusing on the occurrence of micropollutants. The use of market data did significantly increase the chances of identification, since it provided solid evidence that those substances were being actually used in the study area. Therefore, the use of market data may be a valid indicator that helps to obtain a broader picture regarding the presence of micropollutants in the environment. Limitations may arise where countries do not keep or maintain a comprehensive market data register as the one in Sweden.⁸¹

The use of other additional technical criteria to ensure accuracy in analysis of the selected compounds is of paramount importance to obtain high percentage identification rates and be time efficient.

The ratio of tentative identifications in relation to the hits obtained after applying the reduction of feature thresholds was 49% (40% in ESI(+)) and 55% in ESI(-)). In most studies dealing with suspect screening, a much higher percentage identification (however not necessarily in absolute numbers) is achieved in ESI(-) than in ESI(+),^{19,44} because: (i) a much larger number of compounds ionize well in ESI(+) in comparison with ESI(-), (ii) negative compounds tend to show more characteristic fragments (e.g., [O₃S], [HO₄S]) that facilitate their identification, and (iii) the noise in the chromatograms is lower in ESI(-). The fact that the rate of identification in the two modes was almost equal in the present study can be explained by good preselection of compounds and the high number of confirmations carried out with reference standards.

The results in this study clearly show that close collaboration between scientists and regulatory authorities is a very promising way to enhance identification rates and advance knowledge on the occurrence of potentially hazardous substances that are dispersed in the environment. In contrast to previous studies, this work provides semiquantitative information for all confirmed compounds. Achieving a better understanding of the levels of pollutants in WWTP effluent allows sound evaluation of the potential need to monitor these compounds in future studies in, e.g., surface or drinking water. This study did not consider toxicity data in the prioritization approach since the aim was to test the efficiency of a prioritization strategy solely considering a market-based governmental databank. The vast majority of the compounds identified are toxicologically relevant (Table SI-4). However, some substances with low or unknown toxicity were also detected (e.g., stearic acid or tetraethylene glycol). In future prioritization strategies, it would be useful to include toxicity as an additional prioritization factor in order to focus exclusively on the identification of hazardous emerging pollutants.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.7b06598.

Chemical and reagents, instrumental analysis, prioritization, quality assurance and quality control, target analysis of micropollutants, identification of suspects, toxicity of the identified suspects (PDF)

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Notes

The authors declare no competing financial interest.

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