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Semi-quantitative risk-based prioritisation scheme for chemicals of concern in the Nordic countries†

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Exposure to hazardous chemicals can cause adverse effects in humans and the environment. In response to a large number of chemicals potentially emitted to the environment and costly monitoring programmes, prioritisation schemes have been developed to identify candidate substances for further investigation, based on their hazard, exposure and environmental occurrence. Here we present a prioritisation scheme with five filters; persistence/bioaccumulation/toxicity (PBT), hazard, exposure, tonnage, and monitoring, applied to an initial list of 1528 chemicals previously identified as potentially problematic. Based on data on use and detection efforts in the Nordic countries and using a scoring system including scores for data gaps a final list of 16 chemicals was reached. These chemicals are used for instance in adhesives, polyurethane foams, and explosives, and half of them are classified as either acutely toxic or carcinogenic/mutagenic/reprotoxic (CMR) or suspected carcinogenic. With access to data on use amounts and exposure, the prioritisation scheme could be adapted and applied elsewhere. This prioritisation scheme also offers possibilities of more automatisation and thus expansion to a larger group of chemicals as input information to the filters. See graphic below.

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Sustainability spotlight

The production and consumption of chemicals globally is quickly increasing. Today there is registered 204 million chemical structures in the CAS registry. In addition, WHO estimates that 24% of all deaths are linked to environmental exposures and causes. In addition, biodiversity loss in the 6th mass extinction we are currently in – which is accelerated by human impacts. Toxic chemicals play a role – but which ones are most significant? There is hence a need to prioritize chemicals of concern and avoid the most problematic ones and stimulate greening of chemistry. This paper combines both human and environmental hazard data, exposure information of chemicals to support prioritization of compounds of elevated concern. The Organization for Economic Cooperation and Development (OECD) has stressed the importance of developing a strategy to prioritize chemicals to protect public and environmental health. This paper is the first to combine available property data in a semi-quantitative framework to prioritize known problematic chemicals. With this framework it is possible to objectively prioritize chemicals for risk management. This will support the risk management of high-priority chemicals and thereby support the UN SDGs 3 (Good Health); #6 (clean water); #12 responsible production; #14 & #15 (Life under water and on land).

Introduction

Over the past two decades, the number of entries in the Chemical Abstract Service (CAS) database has increased with more than 175 million structures, bringing the total current number up to more than 200 million structures. Although chemicals are an integral part of a modern lifestyle, certain chemicals can cause adverse effects for humans and/or the environment. The World Health Organization (WHO) of the United Nations has estimated that nearly one in four of total global deaths recorded in 2012, or 12.6 million people, could be attributed to living or working in an unhealthy environment, where exposure to chemicals with adverse health effects was identified as a major contributing factor.[1]

In the European Union (EU), approximately 150 000 chemicals were pre-registered for commercial use in 2020, of which more than 22 000 had been registered for manufacture and import in quantities of at least 1 tonne per year.[2] Based on data from the European Environment Agency (EEA) and the European Statistical Office (Eurostat), the United Nations Environment Programme (UNEP) concluded that 62% of the 345 million tonnes of chemicals consumed in the EU were considered hazardous to health[3] although the EEA also noted that the volume of chemicals was not necessarily a proxy for risk.[4] Moreover, chemical pollution might also be related to biodiversity loss, where an estimated 1 million species are under threat of extinction,[5] but the effect of pollution on biodiversity is still studied insufficiently.

Given the large number of chemicals in commerce and potentially emitted to the environment, a prioritisation must

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take place to identify candidate substances for environmental monitoring, risk assessment and management. For instance, the Organization for Economic Cooperation and Development (OECD) has previously stressed the importance of developing a strategy to prioritize chemicals for further risk assessment and/or risk management for individual chemicals, including commercial chemicals, as well as Chemical Substances of Unknown or Variable Composition, Complex Reaction Products and Biological Materials (UVCBs), naturally occurring substances, and new emerging chemicals of concern.[6] The same report also stated that prioritisation decisions should be risk-based.[6]

The European Commission has charted a new long-term vision for the chemical policy of the EU, presented in the EU's Chemical Strategy for Sustainability (CSS) with the political ambition of a zero pollution and a toxic free environment in this decade.[7] These regulator ambitions as well as the substantial resources required for monitoring chemical pollutants further necessitate the development of human and environmental risk-based prioritisation systems for chemicals of concern to facilitate cost-effective environmental monitoring and risk management. Current policies, such as the U.S. Toxic Substances Control Act (TSCA), the Domestic Substance List (DSL) in Canada and the Registration, Evaluation, Authorisation and restriction of chemicals (REACH) in the EU, include different prioritisation approaches but have not been developed for risk ranking of chemicals of potential concern and the subsequent candidate selection.

In this study, we aim to present a semi-quantitative risk-based prioritisation method for chemicals used in the Nordic countries, building on and expanding the previous work by Woldegiorgis *et al.* (2018).[8] In 2021 the authors of this paper produced a report to the Nordic Council of Ministers.[9] This paper presents the report to a wider audience. Furthermore, this case study from the Nordic region also intends to present tools and methods that can be transferred to other parts of the world including individual countries highlighted by the OECD[6] with a focus on revisiting environmental monitoring programmes in terms of revisiting the compounds included in environmental monitoring programs. All data is provided in the ESI† section as an uploaded database – please see this for further details.

Materials and methods

Conceptual approach

This paper reviews chemicals on existing official databases and the data from these. The study includes several lists of chemicals of emerging concern (Table 1) – all reviewed during the first half of 2021 – there are rolling updates to these needs to be take into consideration. It is thus not a review of the literature but a relative ranking of the compounds on the lists. The three REACH lists in Table 1 include chemicals that are subjected to EU regulations, whereas the Community Rolling Action Plan (CoRAP) and List of possible endocrine disrupting chemicals (EDC) include chemicals that have been identified by EU authorities as being of potential concerns. The Substitute It Now! (SIN) list was developed by the International Chemical Secretariat (ChemSec), a government-funded NGO organisation in Sweden, and aims to imply to the industry that chemicals appearing on the list pose a threat to human health and the environment and should as such be replaced as soon as possible. CoRAP and SIN can be considered as lists of chemicals that might be subjected to further regulations in the future. We applied scoring and cut-off values building off the structure of Woldegiorgis *et al.* (2018),[8] however, these can be changed and adapted to the priorities of the user – these are our best scoring suggestions for inspiration.

The prioritisation therefore started from chemicals previously identified as potentially problematic by agencies or organisations, in total 1871 substances from the lists cited in Table 1. Following the OECD recommendation of considering mixtures of chemicals classified as UVCBs in a prioritisation,[6] UVCBs were included in the initial list, whereas metals and intermediate chemicals were omitted, reducing the initial list of chemicals from 1871 to 1528 substances (Table 1).

To develop the final list of prioritised chemicals of these 1528 compounds, five successive semi-quantitative prioritisation filters were applied, which reduced the number of compounds with each filtration step and in combination yielded the total score of each chemical (Fig. 1). The filters and scores assigned to the chemicals in each step were based on Woldegiorgis *et al.* (2018)[8] but used with modification. The first two filters were hazard-based, addressing environmental hazards in terms of Persistence, Bioaccumulation, Toxicity (PBT) and human health or other environmental hazards as they occur on the lists reviewed. The third, fourth and fifth screens were related to exposure characterisation. The absence of information was included and accounted for in the scoring system. The final step of the prioritisation scheme was to summarize the total scores set for each individual chemical passing through all the filters, to generate the final prioritisation list.

Filter 1: persistence, bioaccumulation, toxicity (PBT) profile

The initial prioritisation step (Filter 1) was applied to all the substances on the initial list (Table 1). Table 2 lists the scores for the different PBT property classifications relevant to the hazard characterisation used in the analysis. The scores for each criterion were aggregated to derive the total PBT score.

Chemicals classified as PBT and/or vPvB were assigned the score 1, *suspected* PBT/vPvB were assigned the score 0.7, and *candidate* PBT or vPvB were assigned the score 0.5. In case a chemical was present in more lists than one, the highest score was used. Chemicals with a score ≥ 0.7 progressed to the next filter (Table 3), *i.e.* only compounds classified or suspected as PBT/vPvB. If a compound does not fulfil these criteria, they are deemed not of immediate relative environmental concern warranting costly monitoring and are therefore not progressed in the prioritization.

Filter 2: human and environmental hazards – hazard profile

The second hazard-based filter addressed 27 different hazard properties such as the potential for endocrine disruption or carcinogenicity, mutagenicity, and reprotoxicity (CMR). This filter

Table 1 Lists of chemicals used to generate the initial list of chemicals for the prioritisation scheme as well as weighting factors applied to the scoring in Filter 2

List	Number of entries	Source	Weighting factor
REACH article 59 candidate list	194	(https://echa.europa.eu/en/candidate-list-table)	1
REACH annex XIV authorisation list	55	(https://echa.europa.eu/da/authorisation-list)	1
REACH annex XVII restriction list	125	(https://echa.europa.eu/da/substances-restricted-under-reach)	1
Community rolling action plan (CoRAP) list of the european chemical agency (ECHA)	307	(https://echa.europa.eu/da/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table)	0.5
Substitute it now! (SIN) list	761	(https://chemsec.org/buisness-tool/sin-list)	0.3
List of possible endocrine disrupting compounds (EDC)	430	(https://edlists.org)	0.3
Total	1871		
Subtraction of metals and intermediate chemicals	343		
Initial list for prioritisation	1528		

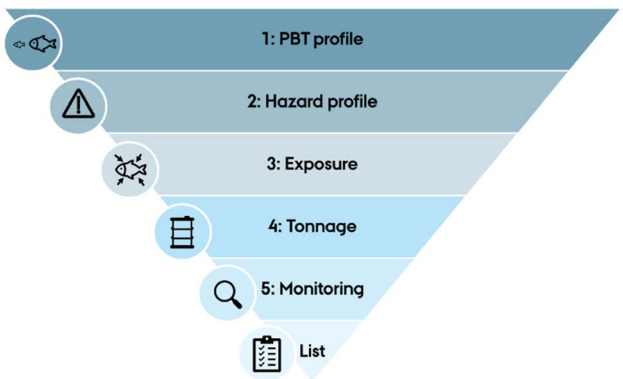

Fig. 1 The five quantitative and successive prioritisation filters used for in this study. PBT: Persistence, bioaccumulation, toxicity.

Table 2 Lists, search term and score for the specific terms used for the PBT filter[a]

List	PBT property classifications	Score
REACH art 59	PBT/vPvB	1
SIN	PBT/vPvB	1
	PBT/vPvB candidate	0.5
CoRAP	PBT/vPvB	1
	Suspected PBT/vPvB	0.7

[a] vPvBs (very persistent and very bioaccumulative).

also scored chemicals according to specific hazard statements of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) such as H350 – May cause cancer and H410 – Very toxic to aquatic life with long lasting effects. The total hazard score points of a chemical were then weighted according to the list of their origin (Table 1). The cut-off score for this filter was set to ≥ 3 (Table 3) for chemicals of concern to progress to the next filter in the prioritisation process. This filter deepens the hazard characterization of the environmentally hazardous compounds from filter 1 with additional toxicity profiling allowing a further sorting of the compounds based on hazard.

Filter 3: total exposure

The two first filters are hazard based; with this filter we add exposure potential at approach a risk based ranking in the subsequent filters. The filter was based on four exposure index tools from the Substances in Preparations in the Nordic Countries (SPIN) database (http://www.spin2000.net/spinmyphp/). This database is a unique and detailed resource for the Nordic countries including use and exposure information for 1000 s of chemicals (31738 records). These tools give a numerical score from 1–5, for the purpose of an initial screening of exposure. The methods behind the assessments and the index values are accessible from the SPIN website. More detailed data regarding certain parameters, such as actual use (indicated as annual tonnage) are needed for a more accurate estimation of environmental and human exposure. The index tools are:

○ Quantity index: this index is based on tonnage of the total use of a chemical registered as a chemical product in the Product Register, normalised against the population size in the Nordic countries. Values are used from 1 to 5, where 5 represents high volume use.

○ Use index: this index provides a general emission/exposure estimation for different human and environmental target groups. The primary recipients/target groups are Surface water, Air, Soil, Wastewater, Consumers, and Occupational groups. The use index gives an indication of the potential "worst case" exposure for each Nordic country since (i) no physical–chemical properties are integrated and therefore the exposure

Table 3 Cut-off values for the filters applied in the prioritisation scheme

Filter	Cut-off value
Filter 1: Persistence, bioaccumulation, toxicity (PBT) screening	≥0.7
Filter 2: Human and environmental hazards	≥3
Filter 3: Total exposure	≥4
Filter 4: Tonnage	≥3
Filter 5: Monitoring results	≥2

estimate represents the local environment at the release source, and (ii) when a substance had several uses with different exposure potential, the index for the most critical usage per target group was used. Values ranged from 1 to 5 for each recipient/target group, where 5 indicates a very probable exposure to that particular chemical.

○ Range of use index: this index indicates the range of the use of a substance in a Nordic country. Values range again from 1 to 5, where 5 indicates a very wide range of applications (number of applications >100).

○ Article index: the article index reflects if a substance is used as part of an article, where a worst-case assumption is employed. For instance, when a substance is used in several articles with different exposure potentials, the index for the most critical usage per target group is selected. Values range from 1 to max 3, where 3 represents very probable use in article productions.

For the purpose of this prioritisation strategy, the Nordic countries were considered as one entity, and the scores were aggregated as presented in eqn (1):

$$\text{Max. exposure value} = \max.(\text{quantity index} + \max.\ \text{use index (surface water, air, soil, wastewater, consumers, occupational)} + \text{range of use index} + \text{article index}) \quad (1)$$

Max. exposure values could range from 4 to 18, and these were in turn assigned scores from 1 to 7. If no information was available for a chemical on exposure, a score of 3.5 was used, which was below the threshold for passing the filter (Table 3). While the original method previously defined by Woldegiorgis *et al.* (2018)[8] only regarded exposure data from Sweden, the current study adapted a pan-Nordic approach. The cut off value for this filter was ≥4 (Table 3), reflecting a max exposure value of 10 or more (calculated according to eqn (1)).

Filter 4: tonnage

The tonnage filter adds an assessment of quantity to the more qualitative exposure filter above thus adding to further ranking of the compounds. The tonnage data used in this filter was also based on data from the SPIN database, *i.e.*, the total use volumes of the identified chemicals including data from the national product registers, reported on a yearly basis, of Norway, Sweden, Denmark, and Finland. The total use volume is calculated according to eqn (2):

$$\text{Total volume} = \text{Production volume} + \text{imported volume} - \text{exported volume} \quad (2)$$

Tonnage data were reviewed for the period of 2013–2018. The highest value was used as a conservative estimate for the Pan-Nordic region. Mixtures that were classified as of "intermediate use only" according to the SIN-list were not considered as relevant for a monitoring programme and thus given a negative score of −40 to efficiently deselect these compounds. If there were only 0 (confidential) or blank (-, or no info) information for tonnage, then the default scoring of 3.5 was used. The cut-off was set for a total use score of ≥3 (Table 3), corresponding to an annual tonnage of 0.0002–0.02 tonnes.

Filter 5: monitoring results

The previous exposure filters are indicators of potential environmental exposure. This last filter adds actual environmental monitoring to the scoring. In the final step of the prioritisation process, chemicals were scored according to their occurrence in the environment based on monitoring data available from the Nordic countries. While Woldegiorgis *et al.* (2018)[8] limited the evaluation of environmental occurrence to monitoring data from Sweden, this study used national databases from Denmark, Norway and Sweden and included some additional information from Finland. The national databases were treated as one entity, *i.e.*, the number of occurrences were combined for all countries. The criterion of occurrence in the environment in the last ten years covered the period 2010–2019. The search included occasional data from air monitoring, but most of the data used for this filter originated from monitoring studies in the aquatic environment from the Nordic countries monitoring databases. We did not include a global review of monitoring and measurements but focussed on the Nordics and their regulatory monitoring programmes as inside the scope of the analysis.

The cut-off value for this filter was ≥2 (Table 3), as opposed to the cut-off value of ≥3.[8] In Woldegiorgis *et al.* (2018)[8] a score of 3 was reached, and thus effectuated that the chemical passed the filter, if it had been analysed and found less than 50 times, based on the consideration that few existing measurements warranted more study. Due to the expanded geographical scope of our approach, even a less studied chemical was often analysed and detected more than 50 times, which would result in a score of 2. If no information was available in the databases for any of the categories, a total score of 7 was reached.

Results and discussion

Filter 1 PBT screening

The first filter scored the chemicals according to their PBT properties, verified or suspected, considerably reducing the

list of chemicals from 1528 to 195 (Fig. 2). It can be argued that focussing on PBT properties might be too narrow for an adequate reflection of current environmental challenges and risks at filter 1. For instance, mobility (M) could be considered included once the data is available and lists include this in the criteria as a hazard criterion in addition as well as very persistent and very mobile (vPvM), are included into REACH legislation.[7] Consequently, the environmental monitoring and related risk assessment of PMT chemicals has received increasing scientific attention.[10–12] Although focussing on PBT criteria, the final list includes some chemicals (Table 4), which are also on a PMT list, *e.g.*, perchloroethylene.[13] However, the first filter could benefit from including mobility as a criterion, together with persistence and toxicity, to account for water-soluble, but less bioaccumulative chemicals once the data is incorporated in the lists.

Filter 2 - human and environmental hazard

The second filter scored the chemicals according to their hazard classification, either based on their hazardous properties, such as a CMR classification, or GHS hazard statements. Of the 195 chemicals passing the first filter, 53 chemicals passed the second filter with regards to total human and environmental hazard.

The scoring of the chemicals was based on the hazard information provided by the lists in Table 1. For instance, the REACH lists compiles data for hazard assessments from various sources such as the eChemPortal (**https://www.echemportal.org/echemportal/**), which in turn includes data from both *in vivo* and *in vitro* experiments as well as regulatory decisions, and the QSAR Toolbox (**https://qsartoolbox.org/**), which contains information from both QSAR models and experimental data are included in the lists. Moreover, published scientific literature is also included in the hazard assessment of chemicals in the REACH lists. It can therefore be argued that the information on the chemicals included in the various lists used as basis for this filter has been extensively evaluated by experts, thus minimising the risk of false positives passing through to the next filter. However, due to this diligence in data evaluation, there may be a possibility that this filter, as well as Filter 1, is too cautious, by omitting emerging chemicals that are currently under assessment but do not fulfil all criteria required for classification of a certain hazard property on the particular list yet, thus generating false negatives that do not pass through to the next filter. As the prioritization focusses on monitoring the prioritized list needs to be sorted to inform cost-effective monitoring.

Filter 3 – total exposure

Similarly, to Filter 1 and 2, the quality of the data included in the SPIN list will significantly affect the outcome of this filtering step. SPIN has built an exposure toolbox, that contains indexes generated and compiled, *e.g.*, from use information stored in the national product registers in the Nordic countries. Out of the 53 chemicals which passed both previous filters, 23 chemicals passed the cut-off for the total exposure filter. Five of the 30 entries that did not pass the filter cut-off, including chemicals such as the polyaromatic hydrocarbon (PAH) benz[*a*]anthracene and the fluorinated chemical perfluorooctanoic acid (PFOA), had a max exposure value of 8. For the remaining 25 chemicals that did not progress to the next filter, no exposure data were available. These included some recognized contaminants such as the fluorinated chemicals perfluorodecanoic acid (PFDA) and perfluorononanoic acid (PFNA) as well as the isocyanate 3,3′-dimethylbiphenyl-4,4′-diyl diisocyanate. Efforts should be made to collect information regarding these data gaps to be able include these compounds in future prioritisation exercises.

Filter 4 - tonnage

All 23 chemicals from filter 3 also passed the fourth filter with a cut-off value of ≥3, disputing the efficiency of this filter. It can be argued that the Quantity Index used as one of the screening tools in Filter 3 – Total exposure and an additional filter for tonnage are redundant. However, the Quantity Index only gives a numerical value (normalised for the population size) from high to low exposure. Filter 4 – Tonnage, on the other hand, provides information about actual amounts of a chemical potentially emitted to the environment. The use of a tonnage filter is also in accordance with the OECD guidelines for prioritisation schemes, stating that regulatory actions for chemicals should be reflected by their increase in use.[6] Moreover, tonnage is an important parameter for the industry with regards to registration under REACH where it is among the standard information requirement to indicate potential exposure.[14] Furthermore, this filter may be used to indicate a trend of increased use of a chemical, if the filter is modified to include a rise in usage over at set time period besides tonnage per year. Nevertheless, it is important to note that use amount alone does not determine the environmental exposure, which will be strongly influenced by the compound's physical–chemical properties.

Filter 5 – monitoring results

Of the 23 chemicals that had passed filter 4, no entries could be found for ten of these chemicals in the national monitoring databases, leading to a default score of 7 (Table 4). Accordingly,

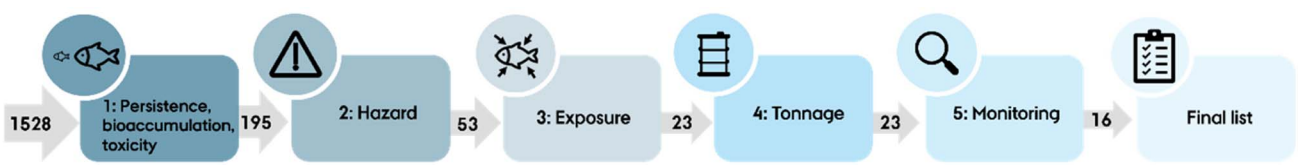

Fig. 2 Summary of the reductions of number of chemicals with each of the five prioritisation filters used for in this study.

Table 4 Score for the chemicals passing through filter 5 – monitoring. Cut-off was ≥2, and the table also includes information as to whether the chemical was included in the report of Woldegiorgis *et al.* (2018).[8] Compounds below *N*,*N*-dicyclohexylbenzothiazole-2-sulphenamide did not pass the criteria for this filter scoring 1

Name	CAS number	EC number	Score filter 5	In Woldegiorgis *et al.* (2018)
m-tolylidene diisocyanate	26471-62-5	247-722-4	7	Yes
6,6′-di-*tert*-butyl-4,4′-thiodi-*m*-cresol	96-69-5	202-525-2	7	Yes
Ethylene dinitrate	628-96-6	211-063-0	7	Yes
1,3,5-tris(oxiranylmethyl)-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione	2451-62-9	219-514-3	7	Yes
1,4,5,6,7,7-Hexachloro-8,9,10-trinorborn-5-ene-2,3-dicarboxylic anhydride	115-27-5	204-077-3	7	Yes
Pigment red 4	2814-77-9	220-562-2	7	No
Diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide	75980-60-8	278-355-8	7	Yes
4-*tert*-butylpyrocatechol	98-29-3	202-653-9	7	Yes
Oxydiethylene dinitrate	693-21-0	211-745-8	7	Yes
1,3,5-Trioxane	110-88-3	203-812-5	7	Yes
Pigment red 3	2425-85-6	219-372-2	3	No
4,4′-methylenediphenyl diisocyanate	101-68-8	202-966-0	2	Yes
Perchloroethylene; tetrachloroethylene	127-18-4	204-825-9	2	No
Tetrabromobisphenol a (TBBPA)	79-94-7	201-236-9	2	No
Musk xylene	81-15-2	201-329-4	2	No
N,*N*-Dicyclohexylbenzothiazole-2-sulphenamide	4979-32-2	225-625-8	2	No
Benzo[def]chrysene = Benzo[*a*]pyrene	50-32-8	200-028-5	1	No
4-Nonylphenol, branched	84852-15-3	284-325-5	1	No
Octamethylcyclotetrasiloxane	556-67-2	209-136-7	1	No
2,2′,6,6′-Tetra-*tert*-butyl-4,4′- methylenediphenol	118-82-1	204-279-1	1	No
Triclosan	3380-34-5	222-182-2	1	No
Chrysene	218-01-9	205-923-4	1	No
Benzo[ghi]perylene	191-24-2	205-883-8	1	No

thirteen chemicals were detected in the national monitoring databases, leading to scores between 1 and 3. The search was challenged by the fact that it proceeded by chemical name in some cases, introducing risks of ambiguity and potentially false negatives. The chemicals passing through this filter are those with a score ≥2, *i.e.*, 16 of the original 23 substances (Table 4). A score of 1 reflected that the chemical had been widely included in the monitoring programmes, and as such presents comparatively little to no knowledge gap.

Given the ambiguity of chemical names, including non-English names, it is essential to provide CAS numbers or other identifiers in databases and other systems intended for search on chemicals. Furthermore, according to the aim of this study, the search on monitoring data was limited to the monitoring databases of the Nordic countries. Future prioritisation schemes can be further extended with monitoring data from other geographically relevant areas. Moreover, countries that lack national monitoring programmes should review and prioritize based on measurements found in the peer-reviewed literature.

Final list

The prioritisation process resulted in a final list of 16 chemicals (Table 5), reduced from the original 1528 substances. The approach of this study includes lists from different bodies and organisations and with different degrees of previous risk assessment. Ensuring this variety in the spectrum of chemicals at the onset of a prioritisation initiative, or even extending it further, may reduce the risk of false negatives. However, the selection of 1528 substances from existing lists only considers compounds with an environmental concern, implying a risk of oversight of chemicals which have not yet been identified as potentially problematic. Alternatively, a prioritisation process could start from all chemicals registered in chemical inventories, as demonstrated by *e.g.*[2,15] approaches, however, are usually faced with the challenges of limited data availability, therefore relying more strongly on modelled chemical properties and environmental behaviour, with the consequences of higher uncertainty in the prioritisation process. Furthermore, in comparison to the extensive prioritisation framework developed by the NORMAN network,[16] the prioritisation scheme presented here offers a tiered ranking of priority of chemicals, rather than identifying the lack of certain data for chemicals arranged in a number of equally prioritised categories.

In this prioritisation scheme, a positive score was added to chemicals with little or no monitoring data. Thus, the lack of sufficient monitoring data can be considered a reason to prioritise a hazardous chemical for monitoring rather than not allowing it to progress through the filters in this prioritisation scheme – hence with the positive score they can still progress.

Development and use of artificial intelligence (AI) as a chemical prioritization resources will allow a higher degree of automatization in the prioritisation process than presented here. This could include harvesting additional lists and databases, as well as automating the real-time updating of the total list ranking.

Metals and intermediates were omitted from the prioritisation scheme during the initial selection of chemicals, and during filter 3 – total exposure, mixtures were removed. However, if the identity of individual components and the

Table 5 Name, CAS and EC-number, total score from the prioritisation process, potential sources, and toxicological profile for the 16 chemicals on the final list

Name	CAS number	EC number	Total score	Potential source(s)	Toxicological profile
m-tolylidene diisocyanate	26471-62-5	247-722-4	23	Used in polyurethane (PU) foams, coatings in floor and wood finishes, sealers, paints, concrete sealers for aircraft and tank trucks and as elastomers[a]	Suspected carcinogen, respiratory sensitising
1,3,5-tris(oxiranylmethyl)-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione	2451-62-9	219-514-3	22.4	Adhesives and sealant chemical, cross-linking agent, intermediates, paint additives and coating additives[b]	Mutagenic
6,6′-di-*tert*-butyl-4,4′-thiodi-*m*-cresol	96-69-5	202-525-2	21.3	Antioxidant in the manufacturing of synthetic rubber and plastics[c]	Potential endocrine disruptor, skin sensitising, PBT
4,4′-methylenediphenyl diisocyanate	101-68-8	202-966-0	20	Used to produce PU foams[d]	Suspected carcinogen, respiratory sensitising, skin sensitising
Diphenyl(2,4,6-trimethylbenzoyl) phosphine oxide	75980-60-8	278-355-8	19.75	Corrosion inhibitors and anti-scaling agents, paint additives, PU coatings[e]	Suspected to be toxic to reproduction, skin sensitising
4-*tert*-butylpyrocatechol	98-29-3	202-653-9	19.6	Paint additives and coating additives, pigments and process regulators[f]	Skin sensitising
Ethylene dinitrate	628-96-6	211-063-0	19.5	Used as an explosive[g]	Sensitiser (eye and skin)
1,4,5,6,7,7-Hexachloro-8,9,10-trinorborn-5-ene-2,3-dicarboxylic anhydride	115-27-5	204-077-3	19.4	Used as a hardener in epoxy resins and a flame retardant in polyester resin, and used in the production polymers for coatings and building materials[h]	Acutely toxic (fatal if swallowed, inhaled, absorbed *via* skin), may cause damage to organs through prolonged or repeated exposure
Pigment red 4	2814-77-9	220-562-2	18.25	Used as dye[i]	Harmful if swallowed or in contact with skin, causes serious eye irritation, may cause long lasting harmful effects to aquatic life
1,3,5-Trioxane	110-88-3	203-812-5	17.45	Used in fungicides, for organic synthesis, as a disinfectant, and in fuel[j]	Eye irritant
Oxydiethylene dinitrate	693-21-0	211-745-8	16.65	Used in explosives[k]	Acutely toxic (fatal if swallowed, inhaled, absorbed *via* skin), may cause damage to organs through prolonged or repeated exposure, harmful effects to aquatic life
Pigment red 3	2425-85-6	219-372-2	16.25	Used in paints, inks, plastics, rubber, cement, textile printing, and munitions[l]	May cause respiratory irritation, very toxic to aquatic life
Perchloroethylene; tetrachloroethylene	127-18-4	204-825-9	15.95	Used in dry cleaning[m]	Suspected carcinogen, skin sensitising
Musk xylene	81-15-2	201-329-4	14.2	Used in perfumes for soap and household products[n]	Suspected carcinogen
Tetrabromobisphenol a (TBBPA)	79-94-7	201-236-9	13.8	Used as a flame retardant additive to plastics, paper and textiles[o]	Carcinogen, under assessment as PBT and endocrine disruptive
N,*N*-dicyclohexylbenzothiazole-2-sulphenamide	4979-32-2	225-625-8	11.7	Curing accelerator for rubbers, fuels and fuel additives[p]	Skin sensitising, under assessment as PBT

[a] https://cameochemicals.noaa.gov/chemical/1613. [b] https://comptox.epa.gov/dashboard/DTXSID4026262#exposure. [c] https://comptox.epa.gov/dashboard/DTXSID4021341#exposure. [d] https://comptox.epa.gov/dashboard/DTXSID7025180#exposure. [e] https://comptox.epa.gov/dashboard/DTXSID4052502#exposure. [f] https://comptox.epa.gov/dashboard/DTXSID5024687#exposure. [g] https://haz-map.com/Agents/489. [h] https://haz-map.com/Agents/1859. [i] https://comptox.epa.gov/dashboard/DTXSID7044637#exposure. [j] https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=as.details&as_id=184. [k] https://haz-map.com/Agents/7837. [l] https://haz-map.com/Agents/4103. [m] https://haz-map.com/Agents/432. [n] https://pubchem.ncbi.nlm.nih.gov/source/hsdb/7692. [o] https://haz-map.com/Agents/3359. [p] https://www.epa.gov/chemicals-under-tsca.

toxicological relevance of these mixtures is further investigated, some of these currently excluded chemicals and/or mixtures should also be included in future prioritisation schemes. Intermediates are considered separately from other chemicals in REACH if it can be ensured that they are produced in controlled closed systems,[17] therefore assuming no emission to the environment. Based on precautionary principles, they could be included in and subjected to a prioritisation scheme to analyse the currently available information.

Table 5 summarises potential sources of the prioritised chemicals, including chemicals used in the polyurethane (PU) manufacturing, as adhesives, pigments, and explosives. Six of the 16 chemicals listed in Table 5 have been classified as either carcinogenic/mutagenic/reprotoxic (CMR) or as suspected carcinogens, and thus have the potential to cause severe adverse health effects. Moreover, two chemicals are acutely toxic and three are classified as endocrine disrupting compounds or are suspected to be endocrine disrupting compounds.

Two chemicals on the final list, *m*-tolylidene diisocyanate (CAS: 26471-62-5), and 4,4′-methylenediphenyl diisocyanate (CAS: 101-68-8) are associated with the manufacturing of rigid or soft PU foams, used for example in insulation materials, soft furnishings. Isocyanates are a family of highly reactive and relatively low molecular weight aromatic and aliphatic chemicals where several are anticipated human carcinogens.[18] Recent findings have indicated that leaching of isocyanate components from plastics might pose an ecotoxicological threat.[19] 1,3,5-tris(oxiranylmethyl)-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione (CAS: 2451-62-9) and diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (CAS: 75980-60-8) have also been associated with PU manufacturing, as a cross-linking agent and PU coating respectively. Thus, besides direct emissions to the environment, the increasing amounts of plastics in the environment may lead to additional sources of contamination.

Conclusions

Considering the current development of new sustainable chemicals policy initiatives in Europe as well as the recognized concern regarding the impact chemicals may have on public health and the environment, including loss of biodiversity and reduction in wildlife abundance, there is a need to address and prioritise the chemicals with highest risk. This paper presents a strategy for a semi-quantitative risk-based prioritisation of chemicals in environmental monitoring campaigns using hazard, use- and exposure-based filters to narrow down the number of candidate chemicals, building on the prioritisation scheme first presented by Woldegiorgis *et al.* (2018)[8] and further developed by Sanderson et (2021).[9] However, as with any prioritisation scheme, the quality of the output, in this case the final list of prioritised chemicals, is dependent on the quality of the input data. For this scheme, we used data sources such as REACH and CoRAP, generally considered to be extensively evaluated, minimising the risk of false positives. However, there might be a possibility that these lists are too cautious if certain compounds do yet fulfil all criteria for inclusion, thus increasing the risk of false negatives.

The proposed prioritisation scheme was applied to data from the Nordic countries and enables governmental agencies and other stakeholders to make more efficient choices when evaluating or initiating risk management including typically time-consuming and expensive environmental monitoring programmes. Where other prioritisation schemes have primarily relied on hazard-based assessments, the combination of exposure and hazard-based filters enables for a more robust method for reviewing data. However, there is a need to further investigate the identity and ratio of chemicals in mixtures considered UVCBs, to include them in future prioritisation schemes.

This prioritisation scheme can be further expanded to other geographical areas if access to data on annual use (tonnage) can be provided or generated. Inventories of chemicals in use should also be established in developing countries, along with tiered rapid prioritisation tools to guide the work with environmental monitoring and risk assessment. Additionally, future studies into developing prioritisation strategies could link the selected chemicals with suggestions of environmental matrices where these chemicals are most likely to occur. Developments in non-target screening techniques should be incorporated in future prioritisation schemes. Moreover, machine learning tools and Artificial Intelligence (AI) should be developed to more effectively harvest toxicological and relevant physical and chemical property data of chemicals from online resources.

Environmental monitoring of chemicals is work and time intensive and thus costly. Monitoring programmes are therefore periodically reviewed for updates to reflect societal and regulatory concerns and priorities. This paper presents a semi-quantitative objective ranking approach of compounds of concern in the European Union. The scoring and cut-offs can be adapted to the user's needs – we provided the Nordic perspective on the scoring and cut-offs. We ended up with 23 compounds as the highest scoring and 16 compounds on the final list. Ten of these are not included in any monitoring programmes in the Nordic region – hence these would be candidates for further analytical investigation and measurement to confirm presence and further inform potential inclusion into environmental monitoring programmes. In addition, compounds on the EU watchlist should be prioritized in accordance with the EU Commission Implementing Decision (EU) 2022/1307. Known problematic compounds such as PFAS are also obvious candidates for consideration based on more qualitative assessments. However, the objective of this paper was to focus on all known problematic compounds and rank these for environmental monitoring and protection purposes.

Author contributions

HS: Funding acquisition; conceptualization; writing – review and editing; formal analysis; methodology; PF: writing – review and editing; formal analysis; LB: writing – review and editing; formal analysis; methodology; visualisation; KV: writing – review and editing; formal analysis.

Conflicts of interest

There are no conflicts to declare.

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