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RESEARCH

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Scoring scheme for Comparative Ranking of impact potential of chemical Alternatives (SCoRA)

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ABSTRACT

Background Replacing hazardous chemicals with safer alternatives is essential for a toxic-free environment. To avoid regrettable substitution, a comparison of the entire spectrum of potential impacts of the candidate for substitution with those of the available alternatives is required. A particular challenge is to also capture yet unknown long-term impacts of (very) persistent chemicals, including but not limited to PBT and CMR properties.

Results For a flexible and transparent comparative ranking of the impact potential of chemical alternatives, we propose a concern-based scoring scheme (Scoring scheme for Comparative Ranking of chemical Alternatives, SCoRA). The approach accounts for hazards due to ecotoxicity in water/sediment and soil, and effects on human health such as CMR properties and endocrine disruption. This is combined with exposure-related information in terms of expected environmental pollution stock levels. The SCoRA approach is illustrated with case study chemicals of very high concern (15 SVHC, mostly PBT, representing different chemical classes with different modes of bioaccumulation and toxicity). A comparison of PBT substances reveals that SCoRA goes well beyond binary screening criteria (PBT: yes/no), showing that PBT substances are all of very high concern, although their impact profiles can be substantially different. Ordinal scores support a detailed characterisation of their potential for long-term impacts. Furthermore, SCoRA enables a coherent comparative assessment of substances with different primary concerns, for example PBT-ness and endocrine disruption.

Conclusions SCoRA complements existing and established tools such as comparative risk assessment. It is particularly useful, when, for example, only limited data are available or when risk assessment is not feasible, as in the case of persistent chemicals. A strength of SCoRA is that the relative contributions of the impact components determining the concern can be visualised with a heatmap and fingerprints. This facilitates communication among scientists, regulators, risk managers, stakeholders and the public.

Keywords Alternatives assessment, Prevention of regrettable substitution, Fingerprinting of concerns, Pollution stock levels representing spatial and temporal dimensions of exposure, REACH, Uncertainties about long-term impacts

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Background

For more than two decades, the European chemicals policy has been striving for an effective protection of ecosystems and human health, leading to a toxic-free environment [1, 2]. Replacing particularly harmful substances such as chemicals with PBT/vPvB ((very) persistent, (very) bioaccumulative and toxic) or CMR (carcinogenic, mutagenic or toxic for reproduction) properties, endocrine disruptors (ED) or persistent, mobile and toxic substances (PMT), has highest priority under the European Chemicals Strategy [3].

Replacing substances of concern with less harmful alternatives requires comparison of the relative impact potential of the candidate for substitution with its alternatives. All possible hazards should be considered to ensure that, for example, a persistent substance is not replaced by a less persistent one but which is an endocrine disruptor. Informed decisions about beneficial or regrettable substitution [4–8] should rely on comparative risk assessment. If this is not possible, other approaches are required, such as for (very) persistent chemicals whose future risks cannot be estimated with sufficient reliability [9], or for substances with relevant data gaps.

A core concern associated with persistent substances is their potential to accumulate in organisms and the environment over time [10, 11]. Increasing environmental stocks cause environmental exposure, and thus the likelihood of adverse effects on human health and ecosystems, to increase over time. In contrast to non-persistent chemicals, negative impacts can continue to occur long after emissions ceased.

Existing frameworks for alternatives assessment [12–14] have largely relied on hazard criteria, in particular H-phrases associated with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) [15]. H-phrases cover physical hazards (200), health hazards (300) and environmental hazards (400). Physicochemical properties, use patterns and exposure pathways can provide information on relative exposure levels [4, 16]. Typically, a comparison of the critical physicochemical properties is sufficient to determine whether exposure is the same, lower or higher for an alternative than for the target chemical. This does, however, not inform about a chemical's expected (long-term) impact or damage potential, which results from the interplay of its hazardous properties and the (long-term) exposure, influenced by its emissions and uses as well as its fate in the environment [17, 18]. The aim of this paper is, therefore, to suggest a more holistic approach to comparative alternatives assessment. We introduce the Scoring scheme for Comparative Ranking of chemical Alternatives, SCoRA, which builds on the internationally agreed approach for prioritizing SVHC [19] and combines different aspects contributing to a chemical's impact potential, including information about intrinsic properties, emissions and expected long-term exposure, effects on human health and ecotoxicity. Our approach extends and complements existing frameworks in several ways. First, in addition to the commonly used parameters for effects and exposure [16], we explicitly include information on the spatial and temporal distribution and accumulation of chemicals in environmental media. This is important to capture potential long-term impacts of persistent substances [1, 10, 17]. Second, SCoRA relies on all available information for a concern-based comparison across chemicals and uses. This goes beyond standard regulatory triggers such as PBTness, which represent multiple hazards with only one binary criterion (PBT: yes/no). By profiling multiple concerns, diverse hazards in relation to the expected exposure are explicitly considered. Third, SCoRA allows comparing chemicals and possible alternatives on an ordinal, continuous scale. Compared to existing approaches, this offers more granular insight into the relative magnitude of impact potentials to support beneficial substitution decisions. Other elements of alternatives assessment, such as technical performance and feasibility, or economic viability are not considered here.

SCoRA is a flexible, transparent and science-based framework for comparing the relative impact potential of different hazardous substances and their alternatives. A particular strength of SCoRA is that it can also be applied to very/extremely persistent chemicals for which conventional risk assessment is not possible.

In the following, we describe the concept of SCoRA and illustrate its applicability with a focus on chemicals with PBT/vPvB properties. The case study chemicals include substances with different use and emission patterns (siloxanes, flame retardants, pesticides), substances with low PBT concern (phenols) and substances with very high PBT concern (PAH, PFAS). We show that the multi-dimensionality of SCoRA facilitates the identification of harmful chemicals. It is thus a tool for comparing chemical alternatives, supporting substitution with safer alternatives while warning against regrettable substitutions.

Materials and methods

Selection of case study chemicals

We chose 15 relatively data-rich substances of concern, particularly PBT substances, to represent different chemical classes with different modes of bioaccumulation and toxicity (Table 1). Three phenols that are SVHC, but not PBT, were included in the dataset to test the discriminatory power of the scoring scheme.

Note that the case study chemicals are well-assessed substances, most of which are already regulated. Based

Table 1 Case study chemicals

Name	CAS	Chem. class	Bioaccumulation	Toxicity	PBTness	References
D4	556-67-2	siloxane	$\mathrm{BCF}_{\mathrm{aquat}}$	Toxic to aquatic and soil biota, CMR	vPvB	ECHA [20]
D5	541-02-6	siloxane	$\mathrm{BCF}_{\mathrm{aquat}}$	Toxic to aquatic and soil biota, indirect effects via food-chain	vPvB	ECHA [20], NIVA [21]
Anthracene	120-12-7	PAH	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota	vPvBT	NIVA [21], ECHA [22], EC [23]
Pyrene	129-00-0	PAH	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota	vPvBT	NIVA [21], EC [23], ECHA [24]
Benzo[a]pyrene	50-32-8	PAH	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, indirect effects via food-chain, CMR	vPvBT	NIVA [21], EC [23], ECHA [25]
Lindane	58-89-9	pesticide	$\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, indirect effects via food-chain, CMR	POP screening criteria fulfilled	NIVA [21], IPCS [26], WFD [27], UNEP [28]
DDT	50-29-3	pesticide	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, indirect effects via food-chain, CMR	Restricted POP	NIVA [21], IPCS [29], Mackay et al. [30], EFSA [31], Kemakta [32]
HBCDD	25637-99-4, 3194-55-6, 134237-50-6, 134237-51-7, 134237-52-8	flame retardant	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, CMR	PvBT	NIVA [21], ECHA [33]
DecaBDE	1163-19-5	flame retardant	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, CMR	PBT/vPvB-forming substance	ECHA [34]
Dechlorane Plus	13560-89-9	flame retardant	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, indirect effects via food-chain	vPvBT	Environment Canada [35], ECHA [36]
PFOA	335-67-1	PFAS	$\mathrm{BAF}_{\mathrm{protein}}$	Toxic to aquatic and soil biota, CMR	PBT	NIVA [21], OECD [37], ECHA [38],
PFOS	1763-23-1	PFAS	$\mathrm{BAF}_{\mathrm{protein}}$	Toxic to aquatic and soil biota, CMR	PBT	NIVA [21], UK Environment Agency [39], EFSA [40], LAWA [41]
Bisphenol A (BPA)	80-05-7	phenol	$\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, CMR, ED	Not PBT	NIVA [21], ECHA [42, 43]
Dimethyl-propyl-phenol	80-46-6	phenol	$\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, ED	Not PBT	UK Environment Agency [44], ECHA [45]
Nonylphenol	84852-15-3, 25154-52-3	phenol	$\mathrm{BCF}_{\mathrm{aquat}}$, $\mathrm{BAF}_{\mathrm{terrest}}$	Toxic to aquatic and soil biota, CMR, ED	Not PBT	NIVA [21], UK Environment Agency [44], ECHA [45, 46], EC [47]

BCF_{aquat} Bioconcentration potential in aquatic organisms and food chains due to log *Kow* > 4.5; $BAF_{terrest}$ Bioaccumulation potential in air-breathing organisms due to log *Kow* > 2 and log *Koa* > 5; $BAF_{protein}$ Bioaccumulation potential in organisms related to protein binding

on the available data and current knowledge, these chemicals are used to test the concept of SCoRA. It is not our aim to re-evaluate their harmfulness or to assess the mutual substitutability of these chemicals.

Properties of case study chemicals

Data were collected from dossiers and assessment reports, for example, from ECHA, EFSA, EU competent authorities, and are presented in the Additional file 1 (Tables S1.1–S1.15). The parameters include physicochemical properties, partition coefficients (log *K*ow, log *K*oa, *K*oc) and bioaccumulation factors, reaction half-lives in air, water, soil and sediment, overall persistence (P_{ov}) and long-range transport potential (LRTP). Toxicological thresholds use predicted no effect concentrations (PNEC) for freshwater, sediment, soil, secondary poisoning and human health via fish consumption, endocrine disruption potential, tolerable daily intake (TDI) and CMR properties (H-phrases).

Some data gaps were tentatively filled with estimates by EpiSuite™ [48]. LRTP and P_{ov} were calculated with the OECD Pov and LRTP Screening tool [49].

Results

We have developed the SCoRA approach to facilitate comparison of the relative impact potential of chemicals for human health and the environment. The approach focuses on components that address gaps in existing methods for assessing chemicals and their alternatives, in particular (1) the assessment of environmental pollution stock levels, which accounts for the spatial and temporal dimensions of environmental exposure; (2) the dual role of persistence as a major driver of the environmental stocks of pollutants over time, and as an important source of uncertainty about future impacts, even after emissions ceased; (3) a composite bioaccumulation score that covers different bioaccumulation metrics for diverse habitats (e.g. aquatic, terrestrial); and, last but not least, (4) tools for communicating the impact potential of chemicals with stakeholders and the public.

Scoring scheme for Comparative Ranking of the relative impact potential of chemical Alternatives (SCoRA)

Impact profiles of chemical substances differ due to differences in persistence, long-range transport potential, bioaccumulation, human health effects and ecotoxicity, according to their different exposure dynamics in water, sediment, soil and air. In SCoRA, both exposure and effects contribute to the overall impact potential (Fig. 1). This makes SCoRA a precautionary approach in which neither low toxicity can compensate for high exposure, nor vice versa.

Hazard and exposure information is translated into ordinal scores of exposure- and effect-related concerns (Eqs. 1 and 2). Weighting factors cover substance- and scenario-related uncertainties regarding the expected pollution burden and, due to overall persistence, yet unknown long-term impacts of substances. The resulting stock and effect scores are then combined into a composite score of a chemical's overall impact potential (Eq. 3).

The stock-pollution approach to characterize exposure-related concerns is an important and novel component of SCoRA and is therefore described in more detail here. The concept of the environmental pollution stock has been widely used in the context of environmental and resource management [18, 50–52]. Generally, the environmental pollution stock denotes the expected amount (mass or concentration) of a chemical in different

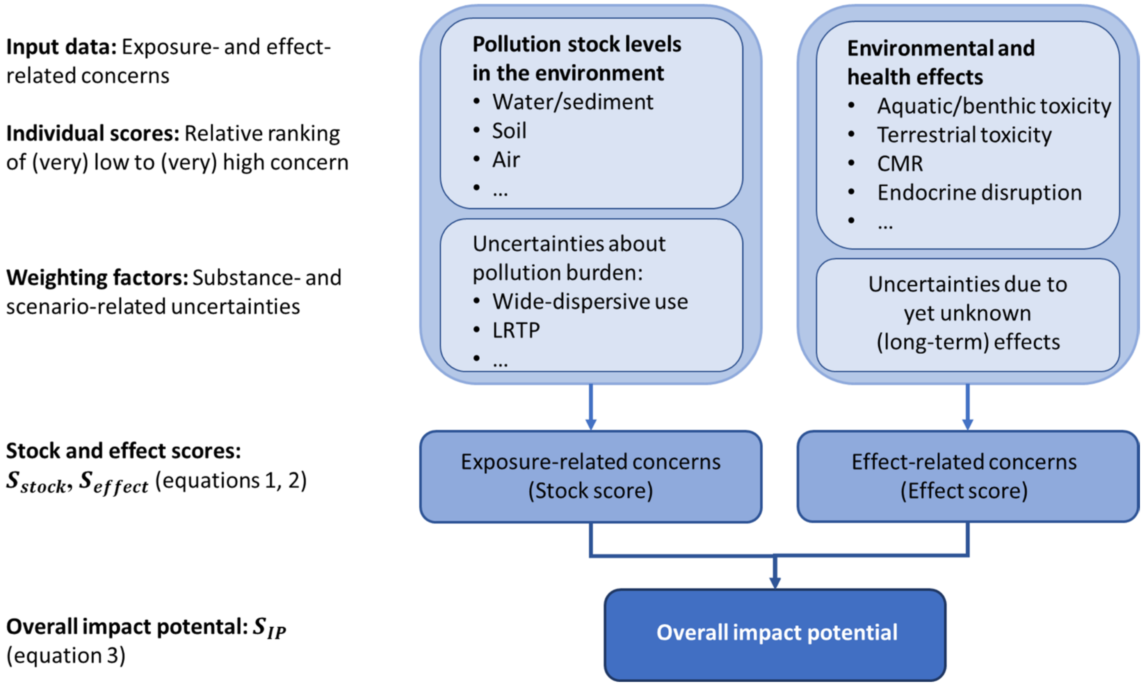


Fig. 1 Schematic outline of SCoRA (Scoring scheme for Comparative Ranking of impact potential of chemical Alternatives) based on concerns related to exposure (stock score) and effects (effect score)

environmental media. If the emission rate exceeds the degradation rate of a chemical ((pseudo)persistence), the environmental stock increases over time, increasing also the impact potential for ecosystems and humans. Moreover, the stock can remain in the environment even long after emissions ceased. While persistence as such is not a hazard parameter, it is obvious that it drives the environmental stock of a chemical, and thus its potential, to cause harm in the short, medium and long term [10, 18].

The environmental pollution stock can be determined using multimedia mass-balance modelling, which integrates information about physicochemical properties, persistence and fate of a chemical and can be applied at different levels of complexity [53–57]. For this study, we used a level III model assuming the same emission signal per period for all chemicals included in the evaluation (for further details and data see Additional file 1: Sect. S3). This results in a projection of the expected stock level in water, soil and biota at steady state [mol], reflecting the expected long-term pollution burden in the environment. In this way, differences between the stocks of chemicals result from differences in their properties and fate, but are not influenced by differences in their (past) use, emissions or environmental conditions. While it is in principle possible to use monitoring data to project the stock based on an existing 'background exposure', this is only meaningful if historic use patterns of the chemicals are similar. If use patterns are different, monitoring data may lead to erroneous conclusions about impact potentials and, hence, misleading conclusions on possible options for substitution.

The stock-score (Eq. 1) captures the concern arising from the expected pollution stock level in water/sediment, soil and biota ($S_{stock(water/sed)}$, $S_{stock(soil)}$, $S_{stock(bio)}$) and informs about the exposure-driven impact potential of a chemical. To address uncertainties about expected stock levels that may be caused by exposure-relevant variables such as the production volume, wide-dispersive use (WDU) and long-range-transport potential (LRTP) of a chemical, we apply a weighting factor ($C_{vol/WDU/LRTP}$).

$$S_{stock} = \left(S_{stock(water/sed)} + S_{stock(soil)} + S_{stock(bio)}\right) * C_{vol/WDU/LRTP} \tag{1}$$

The effect score (Eq. 2) accounts for direct and indirect (along food chains) effects on aquatic and terrestrial organisms including humans, based on ecotoxicological thresholds for water/sediment and soil ($S_{effect(water/sed)}$, $S_{effect(soil)}$), CMR properties ($S_{effect(CMR)}$) and endocrine disruption potential ($S_{effect(ED)}$). Other impacts may be added, for example, if a comparative assessment includes chemicals that are allergens or sensitizers. The weighting factor (C_{Pov}) captures effect-related uncertainties due to yet unknown long-term impacts.

$$\begin{aligned} S_{effect} = &\big(S_{effect(water/sed)} + S_{effect(soil)} \\ &+ S_{effect(CMR)} + S_{effect(ED)} + \ldots\big) * C_{Pov} \end{aligned} \tag{2}$$

Combining the stock and the effect score (Eq. 3) reveals a chemical's overall impact potential, S_{IP}.

$$S_{IP} = S_{stock} * S_{effect} \tag{3}$$

To demonstrate the practical application of SCoRA, we present calculations of S_{IP} for two persistent chemicals, anthracene and benzo[a]pyrene, in the Additional file 1: Sect. S2.1.

Scoring relative stocks and effects

The scaling of the scores is based on categories used in REACH [2], by the US EPA [12] and the GHS for classification and labelling [15] to represent relative hazards from (very) low to (very) high concern (Table 2). In

Table 2 Scores for relative ranking of concerns about chemicals' exposure (stock score) and effects (effect score)

Level of concern	Stock	Effect				Score
	Pollution stock levels in water/sediment* and soil [mol]	Toxicological threshold water, sediment * [mg/L]	Toxicological threshold soil [mg/kg dwt]	CMR properties	ED potential	
–	–	–	–	no	no	0
Very low	< 5	≥ 100	≥ 1000	–	–	1
Low	5–< 50	1–< 100	100–< 1000	–	–	2
Moderate	50–< 500	0.01–< 1	1–< 100	–	low / moderate	3
High	500–< 5000	0.0001–< 0.01	0.01–< 1	H341, H351, H362	–	5
Very high	≥ 5000	< 0.0001	< 0.01	Annex XIII 3.2.3 (d) **	high / very high	10

*Pollution stock levels and toxicities in water and sediment may be considered together based on equilibrium partitioning (EqP) [58, 59].

**Criteria for classification as carcinogenic in Category 1A or 1B (H350 or H350i), germ cell mutagenic in Category 1A or 1B (H340), toxic for reproduction in Category 1A, 1B and/or 2 (H360, H360F, H360D, H360FD, H360Fd, H360fD, H361, H361f, H361d or H361fd), specific target organ toxic after repeated dose in Category 1 or 2 (H372 or H373), according to Regulation EC No 1272/2008.

principle, all relevant hazards should be assessed for the substances to be compared, e.g. according to GHS [15]. If a particular hazard is identified for at least one substance, it should be included in the derivation of an augmented effect score. The option to expand the hazard portfolio assessed in SCoRA by additional hazard endpoints makes the approach sufficiently flexible and applicable to a broad spectrum of chemicals. At the same time, irrelevant hazard endpoints can be omitted. This allows to focus on the critical hazards for the comparative evaluation and ranking. Furthermore, a smaller spectrum of hazard endpoints can be particularly suitable for tailored assessments.

Classifying levels of concern on an ordinal scale provides comparability also between different hazards, such as PBT and ED. In contrast, this is not possible with absolute scales of individual endpoints (e.g. 0–100% effect). The examples of the case studies discussed below illustrate that comparative ranking can work quite well in this way.

The stock scores for water/sediment and soil of the case study chemicals are derived from modelled stock levels [moles] resulting from unit emissions at steady state. Pollution stock levels in water and sediment are considered together based on equilibrium partitioning (EqP) [58, 59]. The resulting values are converted into ordinal scores ranging from 1 to 10 (see Table 2). Note that we assign equal weight to pollution stock levels in water/sediment ($S_{stock(water/sed)}$) and soil ($S_{stock(soil)}$). If other metrics are used to describe the pollution stocks, e.g. dynamic modelling [18], the scoring scales may need to be adjusted accordingly.

Stock levels in air are relevant for greenhouse gases and ozone depleting substances. For most organic chemicals, the air compartment may be important for long-range transport, whereas the accumulation of persistent chemicals in air (causing a pollution stock) is not predominant compared to the other compartments (see also [18]).

The effect scores of the case study chemicals are assigned based on long-term/chronic ecotoxicity data in water/sediment and soil. If compartment-specific toxicity data are available for several relevant endpoints, the lowest value should be preferred. For instance, toxicity data on either direct effects on aquatic organisms or from secondary poisoning of fish-eating predators, including humans can be used for the water compartment. For data-rich substances, a species-sensitivity distribution can be applied to derive an HC5 value (hazardous concentration for 5% of the species) [60]. If data are lacking for certain compartments, extrapolations of values from other compartments are feasible using the tools of the Water Framework Directive (WFD) [59].

CMR properties identified from H-phrases [15] always trigger (very) high concern. Effects on endocrine systems may be already considered in the toxicological thresholds. If not, an additional score ($S_{effect(ED)}$) is required, regarding the range of ED potencies of the chemicals to be compared [61].

Pollution stocks in biota can be assessed indirectly based on the bioaccumulation potential of substances. The bioaccumulation score ($S_{stock(bio)}$) combines different bioaccumulation metrics to cover diverse habitats (e.g. aquatic biota and terrestrial air-breathing organisms) and multiple modes of bioaccumulation (e.g. thermodynamic partitioning, protein binding and membrane binding). Table 3 shows coherent scores corresponding to the respective levels of concern for different bioaccumulation metrics. Combining multiple parameters facilitates a flexible Weight-of-Evidence (WoE) based on all available information, including BCF, BMF [62, 63], physicochemical properties such as log *K*ow and log *K*oa, chemical indicators such as perfluorination for accumulation related to protein binding [64] and elimination half-lives including metabolic transformation [65]. Information from (human) biomonitoring is also conceivable here, but requires a carefully considered scaling of the respective findings.

Table 3 Bioaccumulation metrics and corresponding scores indicating bioaccumulation potential. The composite bioaccumulation score $S_{stock(bio)}$ is the average of the scores assigned to the available bioaccumulation metrics

Level of concern	BCF	BMF	Log *K*ow	Log *K*oa (and log *K*ow > 2)*	Accumulation related to protein binding**	Elimination half-life [d] incl. metabolism***	Score
Very low	< 100	< 0.01	< 1	< 1	no	–	1
Low	100–< 1000	0.01–< 0.1	1–< 2	1–< 4	–	< 70	2
Moderate	1000–< 2000	0.1–< 1	2–< 3	4–< 5	–	–	3
High	2000–< 5000	1–< 2	3–< 4.5	5–< 10	–	≥ 70	5
Very high	≥ 5000	≥ 2	≥ 4.5	≥ 10	yes	–	10

*The log *K*ow > 2 is a prerequisite for accumulation in air-breathing organisms. If log *K*ow is < 2, the respective score for log *K*oa is always 1.

**May be detailed when scales of protein binding related to bioaccumulation will become available.

***According to Goss et al. [65].

The composite $S_{stock(bio)}$ is the arithmetic mean of the scores assigned to available bioaccumulation metrics. It is therefore much more comprehensive than the current assessment criteria, which only consider single aspects of bioaccumulation. This novel approach integrates multiple dimensions of chemicals' bioaccumulation. The resulting level of concern depends on the substances' mode of bioaccumulation, where the same chemical may have different scores for different parameters, e.g. a PFAS with high protein binding but low to moderate partitioning into lipids. To illustrate the procedure for deriving the composite $S_{stock(bio)}$ from different bioaccumulation metrics, we present an exemplary calculation of the bioaccumulation score for anthracene in the Additional file 1: Sect. S2.2.

Weighting factors for stock and effect scores

To capture uncertainties about long-term accumulation of stocks and effects, we introduce weighting factors. Higher uncertainties lead to higher weighting factors. The weighting factor for the stock assessment reflects the relevance of the pollutant stock in water/sediment, soil and biota and is the mean of four individual scores related to production volume (Vol), use pattern (WDU), long-range transport potential (characteristic travel distance (CTD in km) and transfer efficiency (TE in %)) (Table 4). For C_{vol} and C_{WDU} we use the same criteria as recommended by ECHA for SVHC [19]. The LRTP values can be derived using the OECD Pov and LRTP Screening tool [49].

The environmental presence of persistent substances is longer than the duration of established testing methods for environmental and health effects. Uncertainties about long-term effects beyond tested periods shall be covered by a weighting factor based on overall persistence (C_{Pov}). It aims to reflect the increasing likelihood of (very) long-term impacts of (very) persistent substances. P_{ov} can be calculated from the DT50 in air, water and soil using the OECD Pov and LRTP Screening tool [49]. The vP criterion ($t_{1/2} > 180$ d) is a point of reference for assigning C_{Pov} (Table 4).

Level of concern: scaling of the overall impact potential

To compare chemical alternatives, SCoRA offers a scale for relative ranking of substances based on the overall impact potential S_{IP}. Since SCoRA is not a predefined scaffold, but a flexible framework that can be adapted to the range of potential impacts of the substances to be compared, the quantitative (numerical) results of a chemical's impact potential must always be interpreted relative to the impact potentials of other chemicals in the sample, and are specific for any comparative assessment. Thus, the numerical S_{IP} values are not an absolute measure and the associated level of concern depends on possible extensions of Eqs. 1 and 2, for example, when additional human health effects such as respiratory sensitisation are included. By inserting the score values into the respective equations used, the respective S_{IP} values can be easily calculated. For illustration purposes, a detailed example for the calculation of the levels of concern is included in the Additional file 1 with Table S2.3. Here, for the SCoRA set-up with the present Eqs. 1 and 2 and using the scores in Tables 2, 3, 4, Eq. 3 results in a minimum S_{IP} of 6, corresponding to very low concern. Higher S_{IP} values mean more concern:

Table 4 Parameter-related scores for calculating the weighting factors applied to the stock and effect score

Level of uncertainty	Weighting factor components for exposure, pollution burden				Weighting factor for long-term effects	Score
	Production volume	**WDU**	**LRTP (CTD)***	**LRTP (TE)***	**Overall persistence (P_{ov})****	
Very low	< 10 t/y	–	CTD < 5097 km and P_{ov} <195 d	TE < 2.25% and P_{ov} <195 d	< 180 d	1
Low	10–< 100 t/y	IND	–	–	180 days–< 365 days	2
Moderate	100–< 1000 t/y	PROF	CTD < 5097 km and P_{ov} >195 d CTD > 5097 km and P_{ov} <195 d	TE < 2.25% and P_{ov} >195 d TE > 2.25% and P_{ov} <195 d	1 yr–< 5 yr	3
High	1000–< 10,000 t/y	–	–	–	5 yr–< 10 yr	4
Very high	≥ 10,000 t/y	CONS	CTD > 5097 km and P_{ov} >195 d	TE > 2.25% and P_{ov} >195 d	≥ 10 yr	5

WDU: wide-dispersive use (IND: industrial use, PROF: professional use, CONS: consumer use)

LRTP: long-range transport potential (CTD: characteristic travel distance, TE: transfer efficiency)

*Default criteria [49]

**based on vP criterion ($t_{1/2} > 180$ days)

- low concern: S_{IP} between 7 and 96
- moderate concern: S_{IP} between 97 and 729
- high concern: S_{IP} between 730 and 4320
- very high concern: S_{IP} above 4320 up to 30,000

Note that S_{IP} is the product of S_{stock} and S_{effect} (see Eqs. 1–3). Therefore, a high (low) level of concern can result even if one of the two has a low (high) value. In other words: A high environmental exposure of a persistent chemical can trigger a high level of concern even if hazard properties are of moderate or low concern.

Application of SCoRA to the case study chemicals

The proof-of-concept application aims to test SCoRA with real substances and to compare different impact components. Using the substance data in Additional file 1: Tables S1.1–S1.15, we calculated S_{IP} using Eqs. 1–3. The resulting scores for the case study chemicals are detailed in the Additional file 1: Table S2.3.

Figure 2 shows the ordinal ranking of the overall impact potential of the case study chemicals. As expected for SVHC, all S_{IP} are high (above 730) indicating a high level of concern, only D4 has a slightly lower value. The highest value is observed for PFOS, followed by PFOA, DDT, benzo[a]pyrene and dechlorane plus. There are clear differences both between and within substance groups. For these examples with more than tenfold differences in S_{IP}, we choose the logarithmic scale to highlight similar level of concern in the graphical representation. For an alternatives assessment of substances with lower S_{IP}, a linear scale may be more appropriate.

A heatmap of SCoRA results for the case study chemicals (Fig. 3) shows differences, represented by pattern and colour intensity, even between substances with similar S_{IP}. Sorted by S_{IP} (centre column), it shows that all PBT substances are of high concern; however, the impact potentials of PBT substances are not all the same. We see similar rankings in the effect score (right of centre column), regardless of different contributions of environmental and health effects. The stock scoring (left of centre column) reveals a divergent pattern. Often soil is the major sink of persistent substances, but sediments are also affected. The weighting factors indicate high uncertainties about the pollution burden of the case study chemicals ($C_{vol/WDU/LRTP}$ (outer left column)). The uncertainties about long-term effects (C_{Pov} (outer right column)) are correlated with the overall impact potential.

Coping with uncertainties

Limited availability and quality of input data, e.g. degradation rates in different media, can cause substance-related uncertainties. Scenario-related uncertainties may be due to the spatial and temporal scale for assessing pollution stock levels (e.g. local, regional, continental or global). As any data-driven scheme, SCoRA requires sufficient information and consistent coverage of exposure and impact profiles of the chemicals to be compared. Incomplete hazard data in alternatives assessment frameworks can be addressed either by using the

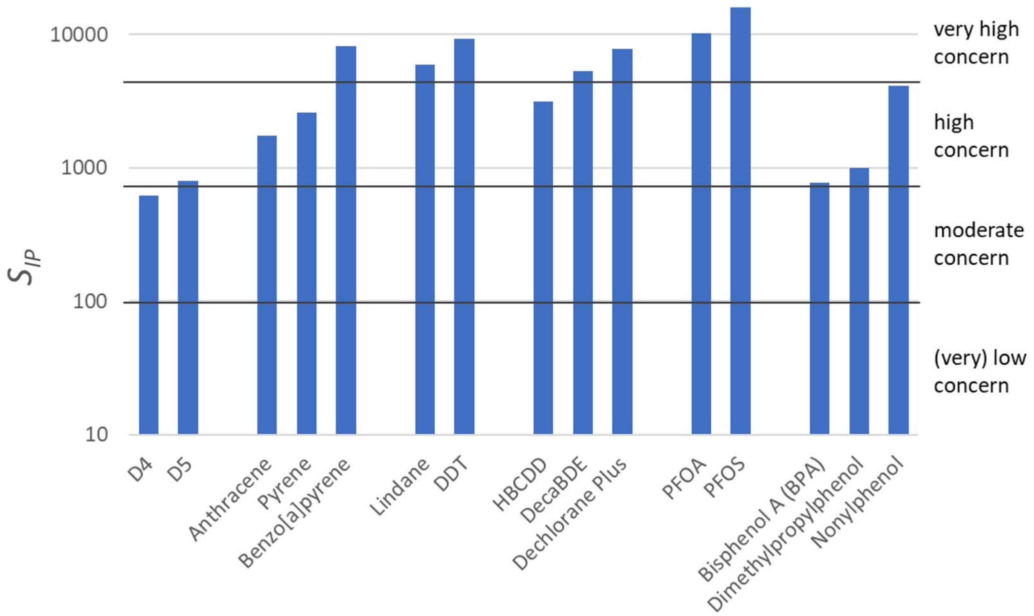
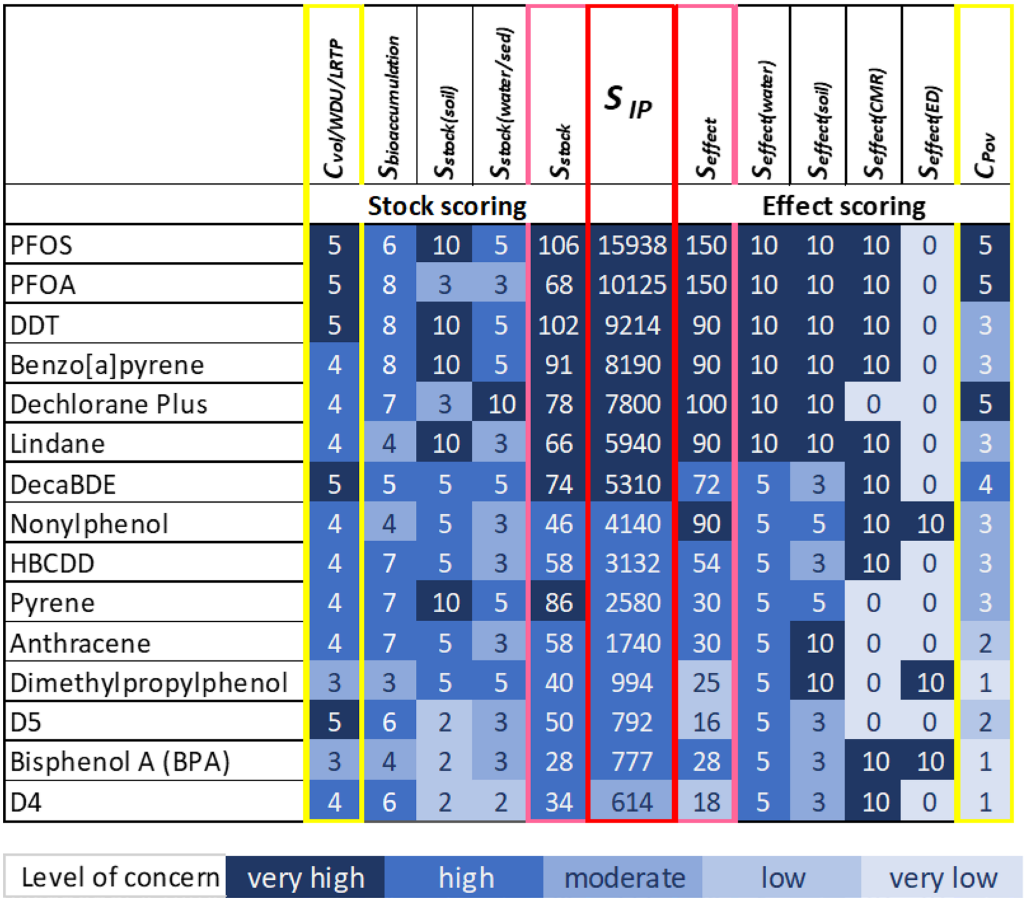


Fig. 2 Overall impact potential S_{IP} of 15 case study chemicals, sorted by chemical class (see Table 1). The horizontal lines indicate level of concern: (very) low concern: $S_{IP} \leq 96$, moderate concern: $S_{IP} \leq 729$, high concern: $S_{IP} \leq 4320$, very high concern: $S_{IP} > 4320$



	$C_{vol/WDU/LRTP}$	$S_{bioaccumulation}$	$S_{stock(soil)}$	$S_{stock(water/sed)}$	S_{stock}	S_{IP}	S_{effect}	$S_{effect(water)}$	$S_{effect(soil)}$	$S_{effect(CMR)}$	$S_{effect(ED)}$	C_{Pov}
		Stock scoring						Effect scoring				
PFOS	5	6	10	5	106	15938	150	10	10	10	0	5
PFOA	5	8	3	3	68	10125	150	10	10	10	0	5
DDT	5	8	10	5	102	9214	90	10	10	10	0	3
Benzo[a]pyrene	4	8	10	5	91	8190	90	10	10	10	0	3
Dechlorane Plus	4	7	3	10	78	7800	100	10	10	0	0	5
Lindane	4	4	10	3	66	5940	90	10	10	10	0	3
DecaBDE	5	5	5	5	74	5310	72	5	3	10	0	4
Nonylphenol	4	4	5	3	46	4140	90	5	5	10	10	3
HBCDD	4	7	5	3	58	3132	54	5	3	10	0	3
Pyrene	4	7	10	5	86	2580	30	5	5	0	0	3
Anthracene	4	7	5	3	58	1740	30	5	10	0	0	2
Dimethylpropylphenol	3	3	5	5	40	994	25	5	10	0	10	1
D5	5	6	2	3	50	792	16	5	3	0	0	2
Bisphenol A (BPA)	3	4	2	3	28	777	28	5	3	10	10	1
D4	4	6	2	2	34	614	18	5	3	10	0	1

Level of concern	very high	high	moderate	low	very low

Fig. 3 Heatmap of the individual scores and overall impact potential of 15 case study chemicals, sorted by S_{IP} (for details see Additional file 1: Table S2.3)

worst case or estimated values [14], the latter for example by read across (from one substance to another) or by extrapolation (from one endpoint to another). Furthermore, ranking with SCoRA remains possible even if one or more endpoints are omitted due to lack of data for all the substances, provided the suspected impact potential is reasonably similar. Another way of dealing with data gaps was developed with the composite score for bioaccumulation. This novel approach allows to derive the level of concern even if the bioaccumulation metrics for the chemicals being compared are different or only partially overlapping. For example, on the basis of BCF for one substance and log *K*ow and elimination half-life for another substance, the respective level of concern with regard to possible accumulation in biota can be deduced and then compared.

To gain insight how data variability may affect the impact scores and the ranking of chemicals, we conducted a sensitivity analysis (for details see Additional file 1: Table S2.4 and Figure S2.4). Even with ± 50% variability in input data, the relative ranking remained unchanged for most chemicals. Where changes in ranking occurred, they were minor (1 or 2 positions). PFOS, PFOA, dechlorane plus, DDT and benzo[a]pyrene scored highest in all scenarios. At the other end of the scale, the scores for D4, D5, bisphenol A and dimethylpropylphenol always remained the lowest. These results indicate that SCoRA provides a consistent ranking of the overall impact potential of chemicals based on various concerns. The robustness of the results is facilitated by the use of ordinal scores for ranges of input data.

To further improve the comparative ranking of chemical alternatives, reference chemicals, i.e. substances with well-known effects, could support the interpretation of impact profiles. Specifically, substances with low, moderate or high impact, e.g. due to carcinogenicity, endocrine disruption or persistence, could help to put both the overall ranking and the impact profile of the substance to be replaced and its possible alternatives into a broader context, similar to internal standards in analytical chemistry. Especially for substances with poor data status, representative reference chemicals would help to improve the robustness and reliability of the relative ranking of impact potential.

Discussion

Substitution of hazardous substances is an effective strategy to reduce their environmental and health impacts [66]. However, an alternative substance, while technically and economically suitable, may potentially be even more harmful than the substance to be replaced [8]. To prevent regrettable substitution, a comprehensive comparative assessment of the full spectrum of properties and effects that contribute to the impact potential of chemical alternatives is required.

The SCoRA approach can facilitate beneficial substitution in several ways. First, ranking chemical substances of concern based on S_{IP} offers a profound way to consider all relevant effects, such as PBT and CMR properties, based on existing data. This allows to identify substances with high impact potential that urgently need to be replaced. Second, SCoRA enables comparative assessment of several substances, such as chemical alternatives. In particular, substances with qualitatively different concern profiles, e.g. a PBT substance and an endocrine disruptor, can be ranked in a coherent and transparent way. Using selected case study chemicals, we show how fingerprinting of impact profiles allows comparison of chemical substances. Furthermore, we discuss why considering estimates of the pollution stock in environmental compartments is important to address the spatial and temporal consequences of persistence.

The first example are two persistent organic pollutants with similar overall impact potential, benzo[a] pyrene ($S_{IP} = 8190$) and dechlorane plus ($S_{IP} = 7800$). Their impact profiles (Fig. 4 A) show clear differences in the scores addressing environmental pollution burden ($S_{stock(water/sed)}$, $S_{stock(soil)}$). Benzo[a]pyrene has very high stock level in soil and somewhat lower, but still high, stock level in water/sediment. For dechlorane plus, the situation is the opposite way, i.e. very high stock level in water/sediment but lower in soil. Concerns about bioaccumulation potential ($S_{stock(bio)}$) are high for both substances, though being slightly higher for benzo[a]pyrene. Maximum scores apply to ecotoxic effects on organisms in water, sediment and soil ($S_{effect(water/sed)}$, $S_{effect(soil)}$). In addition, benzo[a]pyrene has CMR properties (H340, H350, H360FD), but dechlorane plus does not. The comparison of benzo[a]pyrene and dechlorane plus illustrates that the impact profiles of substances with PBT properties are not uniform due to different relative magnitudes of P, B and T as well as other concerns such as CMR. The graphical representation highlights that although PBT substances are all of very high concern, their impact profiles can still be different.

The second example is two SVHC with high overall impact potential, but different primary concern, namely nonylphenol (endocrine disruptor, $S_{IP} = 4140$) and pyrene (vPvBT, $S_{IP} = 2580$). Their exposure- and hazard-related concerns contribute differently to the overall impact potential. This is shown by their impact profiles (Fig. 4B). For nonylphenol, S_{effect} is dominant due to endocrine disruption and CMR properties (H361fd) in addition to ecotoxic effects on organisms in water, sediment and soil. In comparison, pyrene has larger stock levels in soil, water/sediment and biota due to greater persistence. The comparison of nonylphenol and pyrene illustrates that the SCoRA approach allows for a comparative evaluation of different concern categories like PBTness and endocrine disruption in a coherent and transparent way. Using ordinal scores, different impacts that trigger the same level of concern can be compared and aggregated for the evaluation of the overall impact potential.

Exposure-related concerns, reflected by the stock scores, address the spatial and temporal persistence of chemicals in the environment. Environmental pollution stocks aggregate past and current emissions and indicate the pollution burden in different environmental compartments over time. Examples of the relative environmental distribution pattern of the case study chemicals illustrate that different compartments may be the most heavily contaminated (for details and data, see Additional file 1: Sect. S3.2).

The example of PFOS ($S_{IP} = 15{,}938$) and lindane ($S_{IP} = 5940$) can be used to illustrate the possibilities of a comparative exposure assessment based on ordinal stock scores. Their impact profiles (Fig. 4C) reveal the same concerns about very high ecotoxicity and CMR properties. The considerable differences in their overall impact potential are thus due to different exposure characteristics. Depending on the desired level of detail, either the individual compartmental scores or the aggregated S_{stock} can be compared. A major advantage of using pollution stock levels is that both past emissions, from which residues of persistent chemicals are still present in the environment, and current releases are comprehensively taken into account.

SCoRA has been implemented and tested with a selection of well-researched chemicals that are known to be harmful. This proof-of-concept application is, of course, only a small sample of the large number of harmful chemicals for which substitution with safer alternatives is needed. The next step in exploring the applicability of SCoRA to diverse substitution candidates is therefore to broaden the range of chemicals, including emerging substances of concern. Future applications of SCoRA to chemicals with different impacts and uses, for example in

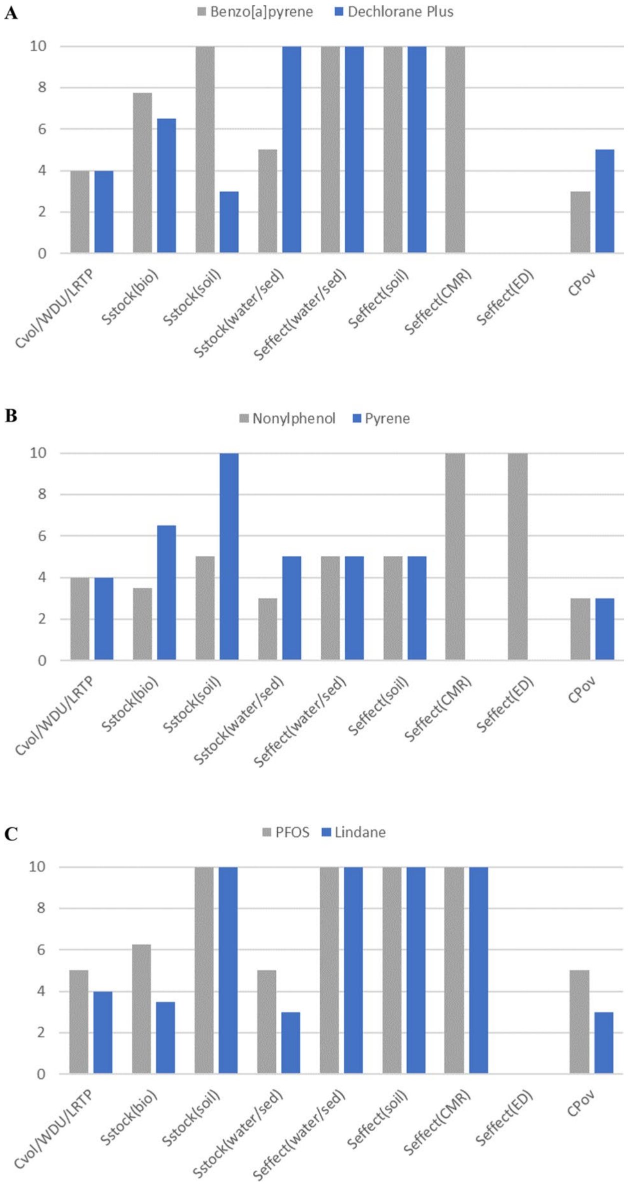


Fig. 4 Impact profiles: Fingerprinting of concerns. **A** Benzo[a]pyrene and dechlorane plus show differences in the impact profile of substances of similar concern with similar overall impact potential (upper diagram). **B** Nonylphenol and pyrene show different concerns of substances with high overall impact potential (middle diagram). **C** PFOS and lindane show same concerns about effects and different exposure characteristics (bottom diagram)

consumer products, will provide useful insights into the robustness of the approach.

Conclusion

Based on the available results, SCoRA has shown to be a transparent and coherent tool for comparing chemical substances across the full spectrum of their potential effects, including but not limited to PBT and CMR properties. SCoRA provides a flexible framework that allows to focus on relevant impacts of the chemicals to be compared. This can contribute to the early detection and thus prevention of regrettable substitution.

SCoRA intends to complement existing and established tools such as comparative risk assessment, when, for example, only limited data are available or when conventional risk assessment is not feasible, as in the case of persistent substances. A strength of SCoRA is the visualisation of multiple concerns by a heatmap and fingerprints, which allow a comprehensive comparison of the potential impacts of different substances. This facilitates communication among scientists, regulators, risk managers, stakeholders and the public about the impact potential of chemicals and their alternatives.

Abbreviations

BAF	Bioaccumulation factor
BCF	Bioconcentration Factor
BMF	Biomagnification factor
BPA	Bisphenol A
CMR	Carcinogenic, Mutagenic or toxic for Reproduction
CTD	Characteristic Travel Distance
D4	Octamethylcyclotetrasiloxane
D5	Decamethylcyclopentasiloxane
DDT	Dichlorodiphenyltrichloroethane
DecaBDE	Decabromodiphenyl ether
DT50	Disappearance Time 50%
ED	Endocrine Disruption
EqP	Equilibrium Partitioning
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HBCDD	Hexabromocyclododecane
HC5	Hazardous Concentration for 5% of the species
log *Koa*	Octanol/Air Partition Coefficient
log *Kow*	Octanol/Water Partition Coefficient
LRTP	Long-Range Transport Potential
PAH	Polycyclic Aromatic Hydrocarbons
PBT	Persistent, Bioaccumulative and Toxic
PFAS	Per- and Polyfluoroalkyl Substances
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctanesulfonic acid
PMT	Persistent, Mobile and Toxic
PNEC	Predicted No Effect Concentration
Pov	Overall Persistence
SCoRA	Scoring scheme for Comparative Ranking of chemical Alternatives
SVHC	Substance of Very High Concern
TDI	Tolerable Daily Intake
TE	Transfer Efficiency
vPvB	Very Persistent and very Bioaccumulative
WDU	Wide-Dispersive Use
WFD	Water Framework Directive
WoE	Weight-of-Evidence

Supplementary Information

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Additional file 1: S1. Properties of case study chemicals. **S2.** Exemplary calculations. **S3.** Assessing the environmental pollution stock to approximate long-term exposure

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Author contributions

Monika Nendza, Stefan Hahn and Silke Gabbert contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript. Michael Klein performed the multimedia fate modelling. Ursula Klaschka improved the applicability of the scheme and participated in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analysed during this study are included in this published article and in additional files.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors have no competing interests to declare that are relevant to the content of this article.

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References

1. van Dijk J, Leopold A, Flerlage H, van Wezel A, Seiler T-B, Enrici M-H, Bloor MC (2021) The EU Green Deal's ambition for a toxic-free environment: filling the gap for science-based policymaking. Integr Environ Assess Manag 17(6):1105–1113. https://doi.org/10.1002/ieam.4429
2. European Commission (2006) REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. European Commission, Brussels, Belgium
3. European Commission (2020) Chemicals Strategy for Sustainability Towards a Toxic-Free Environment. https://ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf.
4. Tickner J, Jacobs MM, Mack NB (2019) Alternatives assessment and informed substitution: a global landscape assessment of drivers, methods, policies and needs. Sustain Chem Pharm 13:100161. https://doi.org/10.1016/j.scp.2019.100161
5. Harremoës P, Gee D, MacGarvin M, Stirling A, Keys J, Wynne B, Vaz S (2001) EEA. Late lessons from early warnings: the precautionary principle 1896–2000. Office for Official Publications of the European Communities, Luxembourg
6. Zimmerman JB, Anastas PT (2015) Toward substitution with no regrets. Science 347(6227):1198. https://doi.org/10.1126/science.aaa0812
7. Maertens A, Golden E, Hartung T (2021) Avoiding regrettable substitutions: green toxicology for sustainable chemistry. ACS Sustain Chem Eng 9(23):7749–7758. https://doi.org/10.1021/acssuschemeng.0c09435
8. Drohmann D, Hernández F (2020) Risk of regrettable substitution under EU REACH: level playing field in the EU regulatory context. Int Chem Regul Law Rev 3(1):25–35. https://doi.org/10.21552/icrl/2020/1/6
9. ECHA (2017) Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment Version 3.0. https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf.
10. Cousins IT, Ng CA, Wang Z, Scheringer M (2019) Why is high persistence alone a major cause of concern? Environ Sci Process Impacts 21(5):781–792. https://doi.org/10.1039/C8EM00515J

11. Conrad JM (2010) Resource economics, 2nd edn. Cambridge University Press, New York
12. National Research Council (2014) A Framework to Guide Selection of Chemical Alternatives. The National Academies Press. https://www.nap.edu/catalog/18872/a-framework-to-guide-selection-of-chemical-alternatives
13. OECD (2021) Guidance on key considerations for the identification and selection of safer chemical alternatives. Environment Directorate, OECD. https://www.oecd.org/chemicalsafety/risk-management/guidance-on-key-considerations-for-the-identification-and-selection-of-safer-chemical-alternatives.pdf.
14. Jacobs M, Malloy TF, Tickner JA, Edwards S (2016) Alternatives assessment frameworks: research needs for the informed substitution of hazardous chemicals. Environ Health Perspect 124(3):265–280. https://doi.org/10.1289/ehp.1409581
15. United Nations Economic Commission for Europe (UNECE) (2019) Globally Harmonized System of Classification and Labelling of Chemicals (GHS). https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev08/ST-SG-AC10-30-Rev8e.pdf.
16. Greggs W, Burns T, Egeghy P, Embry MR, Fantke P, Gaborek B, Heine L, Jolliet O, Lee C, Muir D, Plotzke K, Rinkevich J, Sunger N, Tanir JY, Whittaker M (2019) Qualitative approach to comparative exposure in alternatives assessment. Integr Environ Assess Manag 15(6):880–894. https://doi.org/10.1002/ieam.4070
17. Gabbert S, Hahn S, Klein M, Nendza M, Oosterhuis F (2017) Approach for evaluation of PBTs subject to authorisation and restriction procedures in context of socio-economic analysis. https://publications.europa.eu/en/publication-detail/-/publication/ff4fea17-704d-11e8-9483-01aa75ed71a1/language-en/format-PDF/source-71659651.
18. Gabbert S, de Blaeij A, Quik JTK, Bakker J, de Knecht J, Verbruggen E, Luit R (2022) Can cost-effectiveness analysis of control measures for persistent chemicals be improved? A critical evaluation of approaches for assessing "effectiveness." J Ind Ecol. https://doi.org/10.1111/jiec.13329
19. ECHA (2014) Prioritisation of substances of very high concern (SVHCs) for inclusion in the Authorisation List (Annex XIV). https://echa.europa.eu/documents/10162/13640/gen_approach_svhc_prior_in_recommendations_en.pdf.
20. ECHA (2015) Annex XV restriction report. Proposal for a restriction: octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5). https://echa.europa.eu/documents/10162/9a53a4d9-a641-4b7b-ad58-8fec6cf26229.
21. NIVA (2014) Kvalitetssikring av miljøkvalitetsstandarder. https://www.miljodirektoratet.no/globalassets/publikasjoner/M241/M241.pdf.
22. ECHA (2008) Annex XV-Dossier Anthracene. https://echa.europa.eu/documents/10162/b1ba73fd-44fd-4c4e-8127-203a9a49c51b.
23. European Communities (2008) European Union Risk Assessment Report Coal-Tar Pitch, High Temperature. https://echa.europa.eu/documents/10162/433ccfe1-f9a5-4420-9dae-bb316f898fe1.
24. ECHA (2009) Member State Committee Support Document for Identification of Anthracene Oil, Anthracene-low as a Substance of Very High Concern because of its CMR, PBT and vPvB Properties. https://echa.europa.eu/documents/10162/3e5e6a56-dd4f-4951-b26e-985b7f692624.
25. ECHA (2016) Annex XV – Identification of Benzo[def]chrysene as SVHC. https://echa.europa.eu/documents/10162/75eb6bd5-3375-4d68-854c-138fb87f0067.
26. IPCS (1991) Environmental Health Criteria 124. Lindane. http://www.inchem.org/documents/ehc/ehc/ehc124.htm.
27. WFD (2005) Environmental Quality Standards (EQS) Substance Data Sheet. Priority Substance No. 18 Hexachlorocyclohexanes (incl. Lindane) CAS-No. 608–73–1 (HCHs) CAS-No. 58–89–9 (Lindane). https://circabc.europa.eu/sd/a/e7304cd5-1a9b-49a9-9a22-54bcc8e5510a/18_HCHs-combined_EQSdatasheet_310705.pdf.
28. UNEP (2006) Risk profile on lindane. http://chm.pops.int/Portals/0/Repository/poprc2/UNEP-POPS-POPRC.2-17-Add.4.English.PDF.
29. IPCS (1989) Environmental Health Criteria 83. DDT and its Derivatives – Environmental Aspects. http://www.inchem.org/documents/ehc/ehc/ehc83.htm.
30. Mackay D, Sharpe S, Cahill T, Gouin T, Cousins I, Toose L (2001) Assessing the Environmental Persistence of a Variety of Chemical Substances Including Metals. CEMC Report No. 200104. https://www.researchgate.net/publication/264870293_Assessing_the_Environmental_Persistence_of_a_Variety_of_Chemical_Substances_Including_Metals.
31. EFSA (2006) Opinion of the scientific panel on contaminants in the food chain on a request from the Commission related to DDT as an undesirable substance in animal feed. EFSA J 433:1–69. https://doi.org/10.2903/j.efsa.2006.433
32. Kemakta (2016) Datablad för DDT, DDD och DDE. https://www.naturvardsverket.se/upload/stod-i-miljoarbetet/vagledning/fororenade-omraden/ddtdddochdde.pdf.
33. ECHA (2008) Annex XV dossier Proposal for identification of Hexabromocyclododecane as a SVHC. https://echa.europa.eu/documents/10162/3f5de199-8732-4881-aec6-730bf9499a36.
34. ECHA (2012) Annex XV dossier Proposal for identification of a PBT/vPvB substance. Substance Name: Bis(pentabromophenyl)ether (decabromodiphenyl ether; decaBDE). https://echa.europa.eu/documents/10162/13638/SVHC_AXVREP_pub_EC_214_604_9_decabromodiphenylether_en.pdf.
35. Environment Canada (2016) Draft Screening Assessment. Certain Organic Flame Retardants Substance Grouping 1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-Dechlorane Plus (DP). http://www.ec.gc.ca/ese-ees/FDE6572D-5801-462E-92F7-241FA591DCBF/DSAR_OFRs%20%28DP%29_EN%2002-11-2016.pdf.
36. ECHA (2017) Annex XV – Identification of Dechlorane Plus as SVHC. https://echa.europa.eu/documents/10162/2b729df8-a54f-1485-f77b-185457d96fbd.
37. OECD (2006) SIDS Initial Assessment Report. Ammonium Perfluorooctanoate & Perfluorooctanoic Acid. https://fluoridealert.org/wp-content/uploads/pfoa-april-2006.pdf.
38. ECHA (2013) Annex XV – Identification of PFOA as SVHC. https://echa.europa.eu/documents/10162/5519a346-50f5-4db9-af4e-dd7c520435b4.
39. UK Environment Agency (2004) Environmental risk evaluation report: Perfluorooctanesulphonate (PFOS). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/290857/scho1009brbl-e-e.pdf.
40. EFSA (2008) Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts - Scientific Opinion of the Panel on Contaminants in the Food chain. https://doi.org/10.2903/j.efsa.2008.653. The EFSA Journal (2008) 653, 1–131
41. LAWA (2010) Expertenkreis "Stoffe": Stoffdatenblatt: PFOS CAS 1763–23–1. http://www.laenderfinanzierungsprogramm.de/cms/WaBoAb_prod/WaBoAb/Vorhaben/LAWA/Vorhaben_des_Ausschusses_Oberflaechengewaesser_und_Kuestengewaesser_%28AO%29/O_5.07/index.jsp.
42. ECHA (2008) Annex XV Restriction Report. Bisphenol A. https://echa.europa.eu/documents/10162/13630/trd_uk_bisphenol_a_en.pdf/d7a1ca84-3922-4f4f-b20d-d58241cd4216.
43. ECHA (2017) Registration dossier: 4,4′-isopropylidenediphenol. https://echa.europa.eu/registration-dossier/-/registered-dossier/15752.
44. UK Environment Agency (2008) Environmental risk evaluation report: 4-tert-pentylphenol (CAS no. 80–46–6). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/290845/scho0208bnqr-e-e.pdf.
45. ECHA (2016) Annex XV – Identification of 4-tert-pentylphenol as SVHC. https://echa.europa.eu/documents/10162/6c461b40-cf73-41c4-853c-15d3257d0a2b.
46. ECHA (2013) Annex XV restriction report, Nonylphenol and nonylphenolethoxylates in textiles. https://echa.europa.eu/documents/10162/77e0a60d-fc25-5258-d2f8-a80a9576023a.
47. European Communities (2002) European Union Risk Assessment Report 4-Nonylphenol (Branched) and Nonylphenol. https://mobil.bfr.bund.de/cm/343/4_nonylphenol_und_nonylphenol.pdf.
48. US EPA (2012) Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. United States Environmental Protection Agency. https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface.
49. OECD (2009) The OECD Pov and LRTP Screening Tool 2.2. OECD http://www.oecd.org/env/ehs/risk-assessment/oecdpovandlrtpscreeningtool.htm.

50. Nobbs CL, Pearce DW (1975) The economics of stock pollutants: the example of cadmium. Int J Environ Stud 8(1–4):245–255. https://doi.org/10.1080/00207237608709741
51. Conrad JM, Olson LJ (1992) The economics of a stock pollutant: Aldicarb on Long Island. Environ Resource Econ 2(3):245–258. https://doi.org/10.1007/BF00376199
52. Farzin YH (1996) Optimal pricing of environmental and natural resource use with stock externalities. J Public Econ 62(1):31–57. https://doi.org/10.1016/0047-2727(96)01573-3
53. MacLeod M, Scheringer M, McKone TE, Hungerbuhler K (2010) The state of multimedia mass-balance modeling in environmental science and decision-making. Environ Sci Technol 44(22):8360–8364. https://doi.org/10.1021/es100968w
54. Mackay D, Paterson S (1982) Fugacity revisited. The fugacity approach to environmental transport. Environ Sci Technol 16(12):654A-660A. https://doi.org/10.1021/es00106a001
55. Mackay D, Paterson S (1991) Evaluating the multimedia fate of organic chemicals: a level III fugacity model. Environ Sci Technol 25:427–436
56. Webster E, Mackay D, Wania F, Arnot J, Gobas F, Gouin T, Hubbarde J, Bonnell M. (2005). Development and Application of Models of Chemical Fate in Canada, Modelling Guidance Document. Report to Environment Canada, CEMN Report No. 200501.
57. Di Guardo A, Gouin T, MacLeod M, Scheringer M (2018) Environmental fate and exposure models: advances and challenges in 21st century chemical risk assessment. Environ Sci Process Impacts 20(1):58–71. https://doi.org/10.1039/C7EM00568G
58. Burgess RM, Berry WJ, Mount DR, DiToro DM (2013) Mechanistic sediment quality guidelines based on contaminant bioavailability: equilibrium partitioning benchmarks. EnvironToxicolChem 32(1):102–114
59. European Communities (2011) Technical Guidance for Deriving Environmental Quality Standards. Guidance Document No. 27. Common Implementation Strategy for the Water Framework Directive (2000/60/EC). European Commission. https://circabc.europa.eu/sd/a/0cc3581b-5f65-4b6f-91c6-433a1e947838/TGD-EQS%20CIS-WFD%2027%20EC%202011.pdf.
60. Fox DR, van Dam RA, Fisher R, Batley GE, Tillmanns AR, Thorley J, Schwarz CJ, Spry DJ, McTavish K (2021) Recent developments in species sensitivity distribution modeling. Environ Toxicol Chem 40(2):293–308. https://doi.org/10.1002/etc.4925
61. Segner H, Navas JM, Schäfers C, Wenzel A (2003) Potencies of estrogenic compounds in in vitro screening assays and in life cycle tests with zebrafish in vivo. Ecotoxicol Environ Saf 54(3):315–322. https://doi.org/10.1016/S0147-6513(02)00040-4
62. Gobas FAPC, de Wolf W, Burkhard LP, Verbruggen EMJ, Plotzke K (2009) Revisiting bioaccumulation criteria for POPs and PBT assessments. Integr Environ Assess Manag 5(4):624–637
63. OECD (2017) Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation. https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2017)16&doclanguage=en.
64. Cheng W, Ng CA (2018) Predicting relative protein affinity of novel Per- and Polyfluoroalkyl Substances (PFASs) by an efficient molecular dynamics approach. Environ Sci Technol 52(14):7972–7980. https://doi.org/10.1021/acs.est.8b01268
65. Goss K-U, Brown TN, Endo S (2013) Elimination half-life as a metric for the bioaccumulation potential of chemicals in aquatic and terrestrial food chains. Environ Toxicol Chem 32(7):1663–1671. https://doi.org/10.1002/etc.2229
66. ECHA (2018) Strategy to promote substitution to safer chemicals through innovation. https://echa.europa.eu/documents/10162/13630/250118_substitution_strategy_en.pdf.

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