Multi-Criteria Decision Analysis for Assessments of Chemical Alternatives (MCDA-ACA)

Rachel L. London, Juliane Glüge,* and Martin Scheringer

Institute of Biogeochemistry and Pollutant Dynamics, ETH Zürich, 8092 Zürich, Switzerland

E-mail: juliane.gluege@usys.ethz.ch

Abstract

A comprehensive assessment of chemical alternatives is necessary to avoid regrettable substitution. In a preceding study, an analysis of six hazard assessment methods found that none of them is fully aligned with the hazard assessment criteria of Article 57 of the European REACH regulation, indicating a need for a method better reflecting hazard assessment schemes in European chemical regulations. This paper presents a multi-criteria decision analysis (MCDA) method for the assessment of chemical alternatives (ACA) that takes the criteria of Article 57 of REACH into account. Investigated and presented are objective hierarchies, aggregation of objectives, curvature of the value functions, weights, and the introduction of a classification threshold. The MCDA-ACA method allows for the aggregation of hazards in such a way that poor performance in one hazard cannot be compensated for by good performance in another hazard. The method parameters were developed and tested using two datasets with the aim to classify chemical alternatives into acceptable (non-regrettable) and unacceptable (regrettable) alternatives according to the regulations set in Europe. The flexibility of the general method was explored by adapting the method to align with two hazard assessment schemes, Article 57 of REACH and GreenScreen®. The results

show that MCDA-ACA is so flexible and transparent that it can easily be adapted to various hazard assessment schemes.

Keywords

Multi-criteria decision analysis, assessment of alternatives, regrettable substitution, substance of very high concern (SVHC), minimum aggregation, chemical hazard assessment

Synopsis

We propose parameters for a multi-criteria decision analysis method to comprehensively assess chemical alternatives and present a practical policy tool necessary to prevent regrettable substitutions.

Introduction

Substituting hazardous chemicals is often challenging because the original chemicals have in most cases very specific properties and use areas. In general, three different approaches are available for chemical substitution. One option is a chemical-by-chemical replacement, which is also often called "drop-in chemical replacement".[1] A second option is to find an alternative way of achieving the function of the chemical in the product, for example by redesigning the product or by choosing a different material. Thirdly, a chemical can also be substituted by a change of the system so that the function of the chemical is not required anymore.[1] However, the second and third options are often more complex and may involve higher investment costs. For this reason, a chemical-by-chemical replacement has often been preferred by companies over the other options.[2] Unfortunately, this has also led to regrettable substitutions, where one hazardous chemical has been replaced by another, similar one. To avoid the obstacles of regrettable substitution and "lock-in" of hazardous chemicals, the

potential chemical alternatives should be comprehensively assessed for their hazards before they are introduced into the market.

Jacobs et al.[3] listed several assessment-of-alternative (AoA) frameworks and identified six common components: hazard assessment, technical feasibility assessment, economic assessment, exposure characterization, life-cycle assessment/life-cycle thinking, and decision making. Tickner et al.[4] identified literature gaps and a research agenda to advance the AoA field in the six components listed by Jacobs et al.[3] One of the research needs they identified was to develop decision-making support methods and tools for use in private and regulatory contexts and, specifically, to adapt emerging and existing decision-making support tools for the (aggregation and) weighting of different hazard data. A recent article on this topic (Bechu et al.[5]) concluded that there has been progress in the method and tool development in decision-making. However, it was also stated that further guidance on the use of formal decision-making support tools such as multi-criteria decision analysis (MCDA) for alternative assessment is needed.[5,6]

In London et al.[7], we analysed whether the existing methods for hazard assessment and their decision-making concepts are in line with the hazard criteria of Article 57 of the EU regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). The criteria in Article 57 describe substances that are of very high concern (SVHCs) and may be included in Annex XIV of REACH, which is the list of substances subject to authorization. In London et al.[7], we showed that none of the investigated hazard assessment methods use the same criteria as described in Article 57 of REACH. The same conclusion holds true for the hazard assessment methods that have used MCDA in the past. MCDA is a decision-making support tool that can help decision-makers to choose rationally between multiple options when there are several conflicting objectives (criteria)[8,9]. London et al.[7] concluded that it might be possible to align a method based on MCDA with the criteria of Article 57 on REACH if a more sophisticated objective hierarchy is applied to the hazard criteria.

Several applications of MCDA to the hazard assessments of chemical alternatives have been presented recently.[10–14] However, these studies did not investigate the variability of the results obtained with different MCDA method parameters such as different types of aggregations or different value functions. Typically, equally weighted objectives were assessed in combination with linear value functions and aggregated by taking the arithmetic mean. External regulatory thresholds for hazards, such as a degradation half-life of 180 days for persistent chemicals, were not used and the methods did not reflect the combined hazard criteria used in Article 57 of REACH (e.g., very persistent and very bioaccumulative).

Here we propose an MCDA method based on Multi-Attribute Value Theory (MAVT) with discrete value functions[15] for the assessment of chemical alternatives (ACA), the MCDA-ACA method. MCDA-ACA takes the hazard criteria of Article 57 of REACH into account, but also allows for the integration of various additional objectives, including Global Warming Potential (GWP) and Ozone Depletion Potential (ODP). MCDA-ACA combines the objectives in such a way that poor performance in one objective cannot be compensated for by good performance in another objective. Although the method was initially developed to be applied in the context of the European regulation, it is flexible enough to be applied to other jurisdictions as well. In this paper, the MCDA-ACA method parameters are investigated and set by using a hypothetical substances dataset and subsequently tested using a previously published dataset of real substances data. It is also shown that the objective hierarchy can be adapted to other objectives, such as obtaining the same output as GreenScreen® or mimicking exactly the criteria laid down in Article 57 of REACH. Mimicking GreenScreen® is interesting as GreenScreen® is a decision tree that is recommended and used in various jurisdictions including in the US[16] and the EU.[17] Recreating GreenScreen® makes it also possible to understand whether GreenScreen® has a consistent decision logic through all its hazard classes (called "Benchmarks"). We also provide a Supporting Information (SI) file (SI-3) where the newly developed methods can be used by practitioners in the future.

Methods

Criteria for the development of the MCDA-ACA method

The idea of the MCDA-ACA method is to classify chemical alternatives into acceptable (non-regrettable) and unacceptable (regrettable) substances. This is done by taking the current European chemical legislation, REACH, and objectives recommended in other legislation into account. The objectives selected include with one exception (the physical hazard of flammability) all minimum hazard criteria that were defined by the Organisation for Economic Co-operation and Development (OECD) in 2021 and additionally some of the so called "moving beyond the minimum" criteria of the OECD.[18] One aim is also that the new method can rank the non-regrettable substances according to their hazard. The objectives included are:

- PBT_{eco} and PB, to avoid persistent (P), bioaccumulative (B) and ecotoxic (T_{eco}) as well as very persistent (vP) and very bioaccumulative (vB) substances, in line with the criteria of Article 57 of REACH
- human toxicity (T_{hu}), in order to avoid carcinogenic and mutagenic substances and those that are toxic to reproduction or have other effects on humans such as endocrine disrupting chemicals, in line with the criteria of Article 57 of REACH
- PMT_{eco} and PM, to avoid persistent, mobile (M), and ecotoxic as well as very persistent and very mobile (vM) substances in line with the current CLP regulation
- BT_{eco}, to avoid very bioaccumulative and very ecotoxic (vT_{eco}) substances, in line with the criteria of GreenScreen® for substances that are GreenScreen Benchmark 1 (highest hazard level)
- PT_{eco}, to avoid very persistent and very ecotoxic substances, in line with the criteria of GreenScreen® for substances that are GreenScreen Benchmark 1 (highest hazard level)

- Global Warming Potential (GWP), in order to avoid substances that are potent greenhouse gases
- Ozone Depletion Potential (ODP), to avoid substances that can destroy the ozone layer

Figure 1 shows the objective hierarchy of the MCDA-ACA method, showing how the objectives relate to one another, and the reasons for their inclusion. The thresholds that define when a lower-level objective is actually very high, high, moderate or low are provided in the SI-1, Section S2. The thresholds are based – if available – on the thresholds given in Article 57 of REACH. If no thresholds are available in Article 57, they are based on other relevant European chemical legislation.

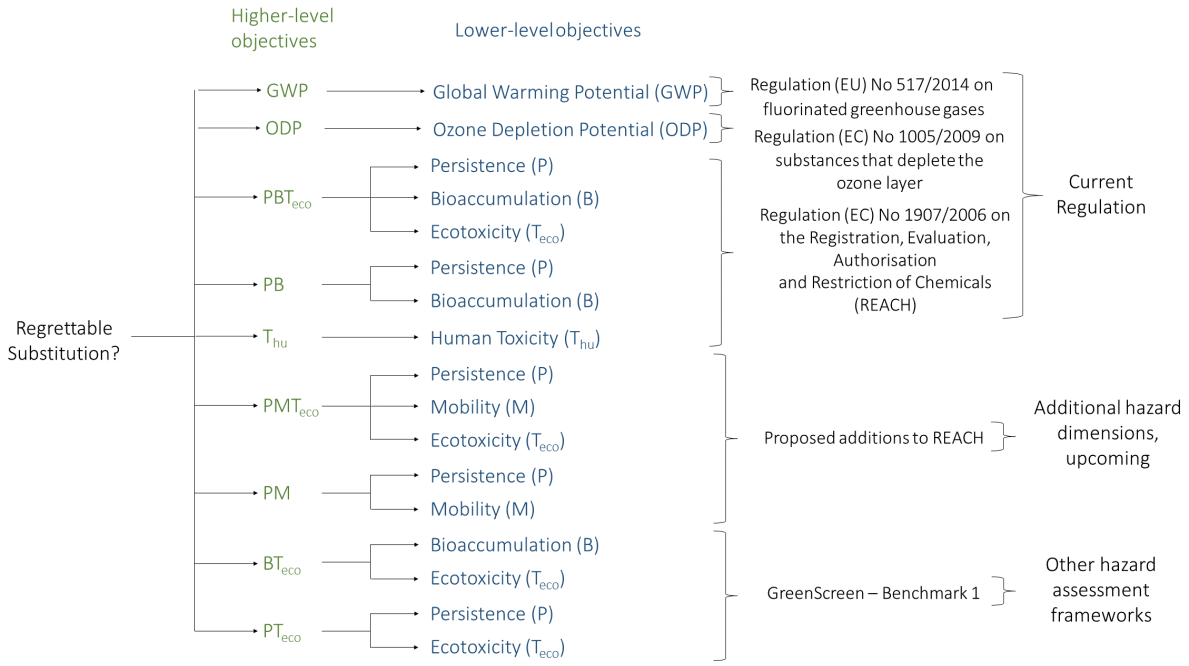

Figure 1: Objective hierarchy of the MCDA-ACA method. GWP and ODP are higher-level objectives that consist of three letters whereas P, B, M, T_{eco}, and T_{hu} are all individual lower-level objectives that are aggregated into various higher-level objectives.

According to the analysis by London et al.[7], a method based on MCDA was deemed useful due to its flexibility and the possibility to explicitly set parameters. The five MCDA parameters that can be varied and are investigated here are the objectives of the assessment (i), the attributes by which these objectives are measured, the value function that is used

to convert these attributes into compatible values (ν_i) for each objective i, the aggregation equation used to combine these values, and, when required, the weights assigned to each objective (w_i). The next subsection explains these terms in more detail.

Introduction to MCDA, Terminology, and Method Parameters

MCDA is a method that assists decision makers in identifying the best alternative in a given context, for a given set of objectives. The objectives are the criteria according to which the alternatives are evaluated. The objectives for any given MCDA should be complete, independent, measurable, concise, without redundancy,[9] and ideally fewer than 15 in number.[19] Exceptions to this rule are possible if minimum or maximum aggregation is used (see below) as this can resolve the redundancy and/or reduce the number of criteria. The relationship between objectives is visually defined in terms of an objective hierarchy (e.g., the lower-level objectives of persistence, bioaccumulation, and ecotoxicity contributing to the higher-level objective of PBT). Objectives are measured by attributes (e.g., degradation half-life of a chemical in water). All attributes are converted into comparable values using a value function, which should have a curvature that reflects the specific preferences of the decision maker. These values are aggregated according to the objective hierarchy and by means of an aggregation logic that reflects the preference of the decision maker. Some aggregation equations necessitate the use of weights, values that quantify the relative importance of objectives.[9] The above terms are referred to in this paper as "method parameters". These method parameters make MCDA a highly flexible method and they should be adjusted to the context of each particular MCDA, including the preferences of the decision maker. Method parameters should also be justified, which makes MCDA a transparent decision-making method. For further definition and explanation of the terms introduced in this section, see SI-1.

Selection of MCDA Method

This paper proposes an MCDA method to assess chemical alternatives, using the MCDA method "Multi Attribute Value Theory" (MAVT) with discrete value functions. There are different types of the MCDA method. To evaluate chemical alternatives within a regulatory context, the MCDA method chosen has to be robust (meaning the result for a given alternative must be independent of the other alternatives included in the analysis). This excludes methods such as AHP, ELECTRE, PROMETHEE, and possibly DSA.[20] MAVT and "Multi Attribute Utility Theory" (MAUT) are both robust methods that can be used when a problem has multiple objectives, with MAVT being a simplified form of MAUT.[21] When the values of attributes are certain, a value function can be used, so MAVT is appropriate. When uncertainty or the risk tolerance of a decision maker needs to be included, a utility function can be used and MAUT is appropriate.[15] In this work, it was found that discrete value functions were required to make the method align with the regulation. Therefore, MAVT rather than MAUT was used in this paper.

Datasets

The MCDA-ACA method parameters were investigated and set by using a hypothetical substances dataset and subsequently tested by means of a previously published set of real substance data. The hypothetical substances dataset is derived from the hazards, and hazard levels, that characterize the identified objectives. The investigated lower-level objectives include P, B, and T_{eco}. The assessment for mobility is the same as for bioaccumulation and it was possible to set the value function, the aggregation and the scaling factor for PMT_{eco} in the same way as for PBT_{eco}. Value function, aggregation and scaling factor for vPvM were set in the same way as for vPvB. Mobility (M) was therefore not added has hazard to the hypothetical substances. Human toxicity (T_{hu}) was added as hazard into the hypothetical substances to see if a higher-level objective with just one lower-level objective could also be included in the same system. Therefore, the hypothetical substances dataset contains

256 combinations (4^4) of the four hazards (P, B, T_{hu}, and T_{eco}) and four qualitative hazard levels (very high, high, moderate, and low). Additionally, for all hypothetical substances, the different hazard combinations were labeled manually as if they were classified according to the regulations shown in Fig. 1. As can be seen in SI-2, 148 of the 256 substances have SVHC characteristics.

The real substance dataset was derived from an MCDA study by Zheng et al.[11], who investigated 16 alternative substances to the flame retardant, decaBDE. There are 20 quantitative attributes in the real substances dataset, including five for persistence, one for bioaccumulation, one for mobility, and 13 for toxicity. Some data points were determined experimentally, others were based on quantitative structure-activity relationships (QSARs). For our assessment, we used the raw data from Zheng et al.[11] in the data gathering step. However, the data normalization was not adopted from Zheng et al.[11], but carried out by us using the thresholds from the Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment.[22] The normalized data were then used to test the data aggregation and data classification. The datasets lacked information on uncertainty; however, this was considered acceptable as the focus of our study was to develop and test a new method.

Steps to use the MCDA-ACA method

The MCDA-ACA method involves five steps until a chemical can finally be classified as acceptable or unacceptable. These steps are data gathering, data normalisation, data conversion, data aggregation, and data classification. The following paragraphs describe these five steps, using the persistence assessment of 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy propanoic acid (HFPO-DA) as an example. Figure 2 shows the corresponding flow chart that includes on the left a general description of the five steps and on the right the steps in the persistence assessment of HFPO-DA.

Data gathering. Attribute data need to be collected for the lower-level objectives of

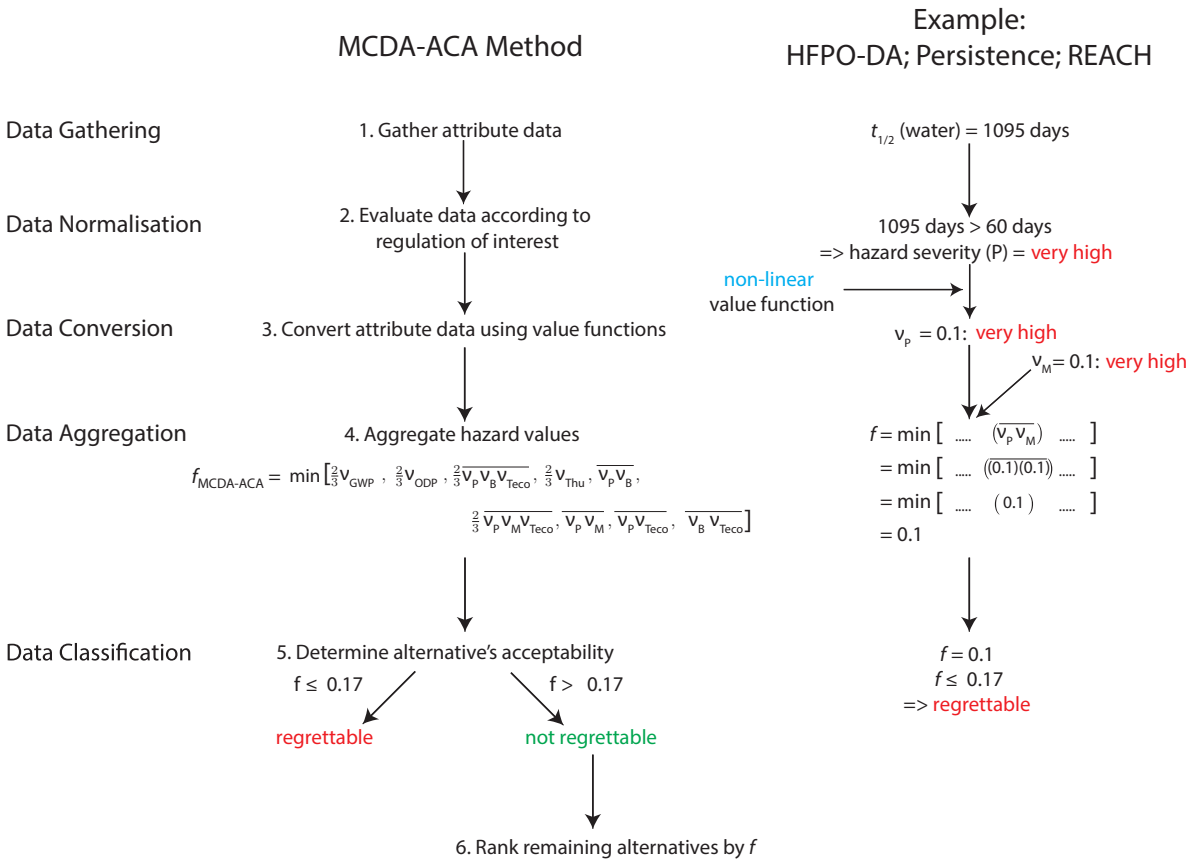

Figure 2: Flowchart showing the MCDA-ACA method. The flowchart on the left shows the general steps, the flowchart on the right the steps for the persistence assessment of HFPO-DA. The notation $\overline{X, Y}$ stands for the arithmetic mean of X and Y.

GWP, ODP, P, B, T_{eco}, T_{hu}, and M. In the example, the attribute "half-life in fresh water" of HFPO-DA was selected as 1095 days[23] and was used for the persistence assessment.

Data normalisation. To ensure alignment of the assessment with relevant regulations, external thresholds are used to categorize the hazard levels of the attributes. Each attribute is categorized into one of the four hazard levels "very high", "high", "moderate", or "low". The individual thresholds that we recommend for MCDA-ACA are given in SI-1 Section S2. For the use of the MCDA-ACA method in the context of European regulation, the thresholds from Annex XIII of REACH[24] are recommended. A category of "high" is given to attributes with half-lives in fresh water above 40 days, whilst a "very high" is given to

those with half-lives in fresh water above 60 days. Therefore, with a half-life in fresh water of 540 days, HFPO-DA would receive the categorization "very high" for this attribute. If the method is intended to be used in other regulations or regions, the thresholds should be adapted accordingly.

Data conversion. Once a hazard level has been assigned to all attributes related to a given objective (i), the hazard levels are converted to a value, ν_i, where $0.0 \leq \nu_i \leq 1.0$, which follow a non-linear (convex) value function. The values are: 0.1 for "very high", 0.25 for "high", 0.6 for "moderate", and 1.0 for "low". Values closest to zero represent the least desirable outcome (highest hazard), whilst values closest to one represent the most desirable outcome (lowest hazard). In the example in Figure 2, for HFPO-DA the attribute of half-life in fresh water would be "very high" according to the threshold in REACH, if this is the only attribute considered for the objective of "persistence", then $\nu_{\mathrm{P}} = 0.1$. If several attributes are available for one objective, then it is proposed to use a minimum aggregation meaning that the worst hazard level of all attributes is selected for the objective.

Data aggregation. The MCDA-ACA method is a mixed aggregation model that uses both additive and minimum aggregation. Additive aggregation is used for the aggregation of lower-level objectives into higher-level objectives. For example, the higher-level objective of (low) PM can be broken down into the lower-level objectives of (low) persistence and (low) mobility, where persistence and mobility are given equal weights. In our example, an additive aggregation (i.e., a weighted average, where each lower-level objective has $w_i = 0.5$), is taken of persistence ($\nu_{\mathrm{P}} = 0.1$) and mobility ($\nu_{\mathrm{M}} = 0.1$), resulting in $\nu_{\mathrm{PM}} = 0.1$.
Minimum aggregation is then used to aggregate the higher-level objectives into an MCDA output for the given alternative, denoted by f. This means that the lowest hazard score of all higher-level objectives is selected as the MCDA output, f, for a given alternative. For HFPO-DA, this results in an $f_{\mathrm{HFPO-DA}} = 0.1$ (not recommended for use as an alternative). The use of minimum aggregation to combine the higher-level objectives prevents poor performance in one objective from being compensated for by good performance in another objective.

Minimum aggregation also ensures that the redundancy in the lower-level objectives does not bias the MCDA output, f.

Data classification. The MCDA output, f, is then used to classify the alternatives in terms of their chemical acceptability. This is done in two ways. Firstly, alternatives with an f below the classification threshold of 0.17 are classified as "regrettable", whilst alternatives with an f above the classification threshold of 0.17 are classified as "not regrettable". The derivation of the classification threshold is explained in the subsection: Parameters of the MCDA-ACA method.

Secondly, once the regrettable alternatives have been removed, the remaining alternatives in the assessment can be ranked in terms of their relative chemical acceptability (i.e., which alternative has a f value closest to 1.0).

Should numerous alternatives be classified as "not regrettable", additional hazards can also be evaluated to differentiate between them. This includes expanding the objective hierarchy to include new objectives (e.g., physical hazards such as flammability, ecotoxicity alone, persistence alone), as well as re-evaluating current objectives with lower thresholds (e.g., lowering the threshold for GWP).

In the example, $f_{\mathrm{HFPO-DA}} = 0.1$ and thus lower than 0.17. HFPO-DA is therefore classified as "regrettable" and would not be recommended to be used as alternative.

Parameters of the MCDA-ACA method

In Eq. 1 the objective hierarchy shown in Fig. 1 and used in the data aggregation step shown in Fig. 2 is formalized: first, the arithmetic means of the ν_i values of the lower-level objectives are taken (denoted by e.g., $\overline{\nu_{\mathrm{P}}, \nu_{\mathrm{B}}}$) and then the lowest hazard score of all higher-level objectives is selected (command "min") as the MCDA-ACA output of the alternative considered:

$$f_{\text{MCDA-ACA}} = \min\left(\frac{2}{3}\,\nu_{\text{GWP}},\ \frac{2}{3}\,\nu_{\text{ODP}},\ \frac{2}{3}\,\overline{\nu_{\text{P}}, \nu_{\text{B}}, \nu_{\text{T}_{\text{eco}}}},\ \frac{2}{3}\,\nu_{\text{T}_{\text{hu}}},\ \overline{\nu_{\text{P}}, \nu_{\text{B}}},\ \frac{2}{3}\,\overline{\nu_{\text{P}}, \nu_{\text{M}}, \nu_{\text{T}_{\text{eco}}}},\ \overline{\nu_{\text{P}}, \nu_{\text{M}}},\ \overline{\nu_{\text{P}}, \nu_{\text{T}_{\text{eco}}}},\ \overline{\nu_{\text{B}}, \nu_{\text{T}_{\text{eco}}}}\right) \quad (1)$$

The scaling factor of 2/3 is explained below. To ensure that the MCDA-ACA method correctly reflects the regulation and guidance referred to in Fig. 1, the method parameters need to be optimized, including the curvature of the value function (for the data conversion step), the inclusion of a scaling factor, here 2/3 (for the data aggregation step), and the classification threshold (for the data classification step).

The parameters were optimized by comparing the known labels of "regrettable" vs. "not regrettable" for the set of 256 hypothetical chemicals with the MCDA-ACA output for the same chemicals, and refining the MCDA-ACA parameters until agreement between the labels and the MCDA-ACA output was reached. An important consideration here was that the hazard combination of high P, high B and high T_{eco} should have – according to Article 57 of REACH – the outcome "regrettable" while at the same time very high P, high B and moderate T_{eco} should be "not regrettable". This is only possible if a non-linear (convex) value function is used. The reason is that, with a convex value function, the differences between the values increase from very high to high to moderate and low. The average of very high, high and moderate thus has a higher score with the convex value function (the score would be 0.317 if 0.1, 0.25, and 0.6 are used for very high, high and moderate, respectively) than the average of high, high and high (score 0.25). With a linear value function, the score in both examples would be 0.25. A convex value function was therefore chosen for MCDA-ACA. Finding suitable discrete values for the convex value function was done manually by using Table 1 and is described in detail in the SI-1 Section S3.1. The final hazard values are 0.1, 0.25, 0.6, and 1 for very high, high, moderate, and low, respectively.

The derivation of the classification threshold and the scaling factor of 2/3 for some of the higher-level objectives can be understood by looking at Table 1. All hazard combinations that are listed under "regrettable" in Table 1 need to have a score that is lower than the score for the hazard combinations that are listed under "not regrettable". Which hazard combinations fall under "regrettable" and which under "not regrettable" is defined by Article 57 of REACH and the other European Regulations, which are given in Fig. 1.

When looking at the hazard combinations that have two lower-level objectives (PB, PT_{eco}, BT_{eco}, PM), one can see that the lowest score for the "not regrettable" hazard combinations is 0.175. This means that all scores for the "regrettable" hazard combinations need to be lower than 0.175. However, hazard combinations such as high P, high B and high T_{eco} or high T_{hu} that describe regrettable substitutes according to Article 57 of REACH would get a score of 0.25 as the average hazard level is "high". The scaling factor lowers this score to 0.167 and is therefore needed to ensure the correct classification of the hazard combinations. For more information see SI-1 Section 3.2.

The highest score for the regrettable hazard combinations obtained is therefore 0.167, the lowest score for the non-regrettable hazard combinations is 0.175. A classification threshold of 0.170 can therefore separate regrettable and non-regrettable hazard combinations. Importantly, the scaling factor should not be confused with a weighting factor that is sometimes needed in other MCDA models. The use of minimum aggregation at the higher-level objectives does not require any weighting factors here.

Table 1: Higher-level objectives of the MCDA-ACA method, with examples of regrettable and non-regrettable hazard combinations, together with their corresponding score. The value function is non-liner and convex (very high (v) = 0.1, high (h) = 0.25, moderate (m) = 0.6, and low (l) = 1.0). "x" indicates high-level objectives where the factor of 2/3 was included.

	Regrettable		Not Regrettable		
Higher-level objectives	**Hazard combinations**	**Score**	**Hazard combinations**	**Score**	**Factor 2/3**
PBT_{eco}	hP, hB, vT_{eco}	0.13	vP, vB, mT_{eco}	0.178*	x
	hP, hB, hT_{eco}	0.167	vP, hB, mT_{eco}	0.21	x
			hP, hB, mT_{eco}	0.24	x
T_{hu}	vT_{hu}	0.07	mT_{hu}	0.4	x
	hT_{hu}	0.167			x
PB	vPvB	0.1	vP, hB	0.175	
			vB, hP	0.175	
			hP, hB	0.25	
PT_{eco}	vP, vT_{eco}	0.1	vP, hT_{eco}	0.175	
			vT_{eco}, hP	0.175	
			hP, hT_{eco}	0.25	
BT_{eco}	vB, vT_{eco}	0.1	vB, hT_{eco}	0.175	
			vT_{eco}, hB	0.175	
			hB, hT_{eco}	0.25	
PMT_{eco}	hP, hM, vT_{eco}	0.13	vP, vM, mT_{eco}	0.178*	x
	hP, hM, hT_{eco}	0.167	vP, hM, mT_{eco}	0.21	x
			hP, hM, mT_{eco}	0.24	x
PM	vPvM	0.1	vP, hM	0.175	
			vM, hP	0.175	
			hP, hM	0.25	
GWP	vGWP	0.07	mGWP	0.4	x
	hGWP	0.167			x
ODP	vODP	0.07	mODP	0.4	x
	hODP	0.167			x

* This combination of lower-level objectives is covered by another higher-level objective.

Creating MimicREACH and MimicGreenScreen

In order to show that the MCDA-ACA method can be tailored to other decision logics and objective hierarchies, two additional MCDA methods were created, MimicREACH and MimicGreenScreen. The aim of MimicREACH is to classify chemical alternatives into substances that meet the criteria for SVHCs as defined in Article 57 of REACH and those that do not meet the criteria. MimicGreenScreen intends to classify chemical alternatives according to the four benchmark categories that are defined in Annex 3 of GreenScreen®.[25]

As a first step, objective hierarchies were created using the lower-level objectives identified in Article 57 of REACH[24] and in Annex 3 of GreenScreen®.[25] Secondly, an aggregation equation was created for both models. Finally, the data classification step was carried out to replicate the original methods.

Results

MCDA-ACA

With the objective hierarchy given in Figure 1, it was possible to find suitable MCDA method parameters (see SI-2 "MCDA-ACA method - Hyp. Subs"). Of the hypothetical substances, 61% were classified as "regrettable" ($f \leq 0.170$), whilst 39% were classified as "not regrettable" ($f > 0.170$). All substances that would be classified as SVHC under REACH were also classified as "regrettable" by MCDA-ACA. For 3% of the substances, MCDA-ACA considered their hazard combinations "regrettable", whilst they would not be classified as SVHC under REACH. Specifically, this occurred for substances with the hazard combinations $\mathrm{vPvT_{eco}}$ and $\mathrm{vBvT_{eco}}$.

Within the group of hypothetical substances classified as "not regrettable", certain substances still have a single "very high" hazard. This occurs where a hazard is not included individually as a higher-level objective, but combined (averaged) with other hazards in the

formation of higher-level objectives, see Figure 3. For example, Substance 64 in SI-2 (vP, lower-level, $f = 0.47$) is classified as "not regrettable", whilst Substance 253 in SI-2 ($\mathrm{vT_{hu}}$, higher-level, $f = 0.07$) is classified as "regrettable". For all results, see SI-2 "MCDA-ACA method - Hyp. Subs". Important to note here is that the assessment was only conducted with the lower-level objectives P, B, T_{eco}, and T_{hu}. If the substances represented real world examples, those that were deemed non-regrettable would also need to be evaluated for M as well as GWP and ODP to confirm that they are really non-regrettable. When the MCDA-ACA method was applied to the 17 real substances, all substances were classified as "regrettable" ($f \leq 0.170$). However, there was some small variation in f amongst the alternatives ($0.07 \leq f \leq 0.10$), indicating that some alternatives were worse than others. For all results, see SI-2 "MCDA-ACA method – Real Subs."

Practitioners who would like to use the MCDA-ACA method on their own, can use the "MCDA-ACA method - forUsers" in the SI-3. The structure of the sheet is similar to that in the SI-2, except that users can enter their own data (hazard severities) here and that there are further instructions as to where which values must be entered.

MimicREACH

A small number of adjustments to the MCDA-ACA method made it possible to replicate the decision logic of the hazard assessment according to Article 57 of REACH, see also SI-2 "MCDA - MimicRACH". The objective hierarchy is shown in Figure 3a). The main change is that fewer higher-level objectives were included in the objective hierarchy than for MCDA-ACA. The corresponding aggregation equation is given in Eq. 2.

$$f_{\mathrm{mimicREACH}} = \min\left(\frac{2}{3}\,\overline{\nu_{\mathrm{P}}, \nu_{\mathrm{B}}, \nu_{\mathrm{T_{eco}}}},\ \frac{2}{3}\,\nu_{\mathrm{T_{hu}}},\ \overline{\nu_{\mathrm{P}}, \nu_{\mathrm{B}}}\right) \tag{2}$$

The value functions and the classification threshold for SVHC vs. not SVHC are the same as in MCDA-ACA. When applied to the 256 hypothetical substances, MimicREACH

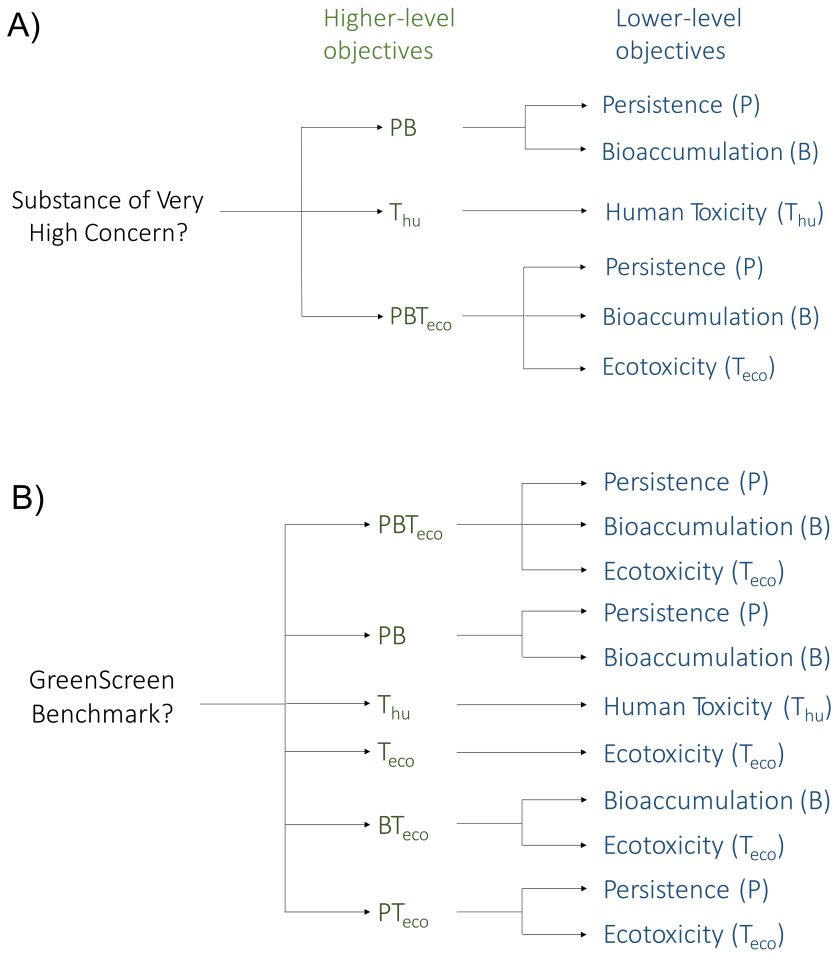

Figure 3: Objective hierarchy of a) MimicREACH and b) MimicGreenScreen

correctly identifies all 148 SVHCs. An implementation of MimicREACH in MS Excel is provided in the SI-3 under ´´MCDA - mimicREACH - forUsers".

MimicGreenScreen

With MimicGreenScreen, we intend to replicate the decision logic of GreenScreen®. The objective hierarchy is shown in Figure 3b. The main difference from MCDA-ACA is that PMT_{eco}, PM, GWP and ODP are not included as higher-level objectives in MimicGreenScreen while T_{eco} is added additionally. The parameters include again a mixed aggregation hierarchy (additive and minimum), non-linear (convex) value functions, and equal weighting for the lower-level objectives. Because there are four so-called benchmarks in GreenScreen®,

three classification thresholds are needed instead of one in MCDA-ACA. The thresholds were set at 0.170, 0.41 and 0.65 (the derivation of the thresholds is shown in the SI-1 Section S4) and the aggregation equation is shown in Eq. 3.

$$f_{\mathrm{mimicGS}} = \min\left(\frac{2}{3}\,\overline{\nu_{\mathrm{P}}, \nu_{\mathrm{B}}, \nu_{\mathrm{T_{eco}}}},\ \frac{2}{3}\,\nu_{\mathrm{T_{hu}}},\ \overline{\nu_{\mathrm{P}}, \nu_{\mathrm{T_{eco}}}},\ \overline{\nu_{\mathrm{P}}, \nu_{\mathrm{B}}},\ \overline{\nu_{\mathrm{B}}, \nu_{\mathrm{T_{eco}}}}, \nu_{\mathrm{T_{eco}}}\right) \tag{3}$$

With these parameter combination and thresholds, 89% of the hypothetical substances were classified consistently with GreenScreen®. This is an important finding which shows that the decision logic of GreenScreen®, in large parts, has a consistent structure that can be replicated with an MCDA approach. At some points, however, GreenScreen® contains ad-hoc weightings of certain hazards that cannot be replicated by the value functions underlying MimicGreenScreen and, therefore, lead to different results for MimicGreenScreen and GreenScreen®. Some of these cases are shown in Table 2. These cases are characterized as follows:

- Substances with PBT or even vPBT properties, but low human toxicity are only Benchmark 2 in GreenScreen®, but Benchmark 1 in the MCDA decision logic: here, GreenScreen® requires very high T_{eco} in addition to (v)PB for the substances to be Benchmark 1 (6 substances, rows 1 and 2 in Table 2)

- Substances with very high ecotoxicity, both alone and in combination with other hazards, are only Benchmark 2 in GreenScreen®, but Benchmark 1 in the MCDA decision logic (16 substances; rows 3 and 4 in Table 2)

- Substances with high ecotoxicity, low human toxicity and low or moderate P and B, are only Benchmark 3 in GreenScreen®, but Benchmark 2 in the MCDA decision logic (3 substances, row 5 in Table 2)

- Four specific cases where GreenScreen® and the MCDA decision logic assign Benchmarks 2 instead of 3 and vice versa (rows 6 to 9 in Table 2)

Regarding the Benchmarks 2 to 4 of GreenScreen®, there is no clear "right" or "wrong" as there is no legal reference point for these substances. However, substances that are Benchmark 1 in MimicGreenScreen, such as PBT substances, would potentially be classified as SVHCs under REACH and we therefore think that Benchmark 1 (Avoid – chemical of high concern) is more appropriate in this case than Benchmark 2 (Use, but search for safer substitute).

Table 2: Selected examples of MimicGreenScreen and GreenScreen® benchmarks from the hypothetical dataset, where 1 = "Avoid - chemical of high concern", 2 = "Use but search for safer substitutes", 3 = "Use but still opportunity for improvement", 4 = "Prefer – Safer chemical"

Substance No.	P	B	T_{eco}	T_{hu}	Mimic GreenScreen	GreenScreen® Benchmark
88	high	high	high	low	1	2
24	very high	high	high	low	1	2
99	high	moderate	very high	moderate	1	2
244	low	low	very high	low	1	2
184	moderate	low	high	low	2	3
124	high	low	moderate	low	3	2
220	low	high	moderate	low	3	2
48	very high	moderate	low	low	2	3
144	moderate	very high	low	low	2	3

Effect of different objective hierarchies

It has been argued that persistence alone is a major cause for concern.[26] If decision makers would like to include persistence alone in MCDA-ACA, they would need to add P as higher-level objective (see SI-2 – MCDA-ACA+P). As a consequence, some additional hypothetical substances would be classified as regrettable. Figure 4 shows the distribution of the MCDA outputs (f) of the hypothetical substances dataset when the dataset is assessed according to the three different objective hierarchies of MimicREACH, MCDA-ACA, and MCDA-ACA+P. As the distribution shifts from MimicREACH to MCDA-ACA and finally to MCDA-ACA+P, a greater share of the distribution (and therefore hazard combinations) lies below the categorisation threshold of $f = 0.17$ and is therefore categorised as

"regrettable". Figure 4 also gives the example of two non-SVHC hazard combinations whose categorisation changes from "not regrettable" to "regrettable" as the objective hierarchy expands to include more hazard combinations. The first hazard combination describes very bioaccumulative and very ecotoxic ($vBvT_{eco}$) substances that have low hazards in the other endpoints. The second one represents a very persistent (vP) substance with low hazards in the other endpoints.

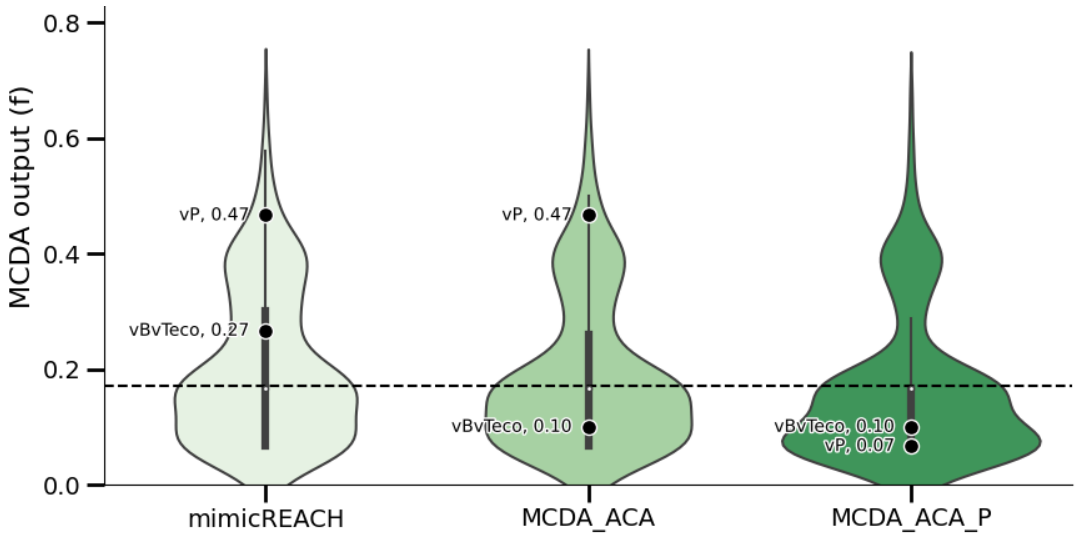

Figure 4: Distribution of MCDA output (f) for the different objective hierarchies of MimicREACH, MCDA-ACA, and MCDA-ACA+P. The distribution of f was calculated for the hypothetical substance dataset. Two hazard combinations are highlighted: $vBvT_{eco}$ (very bioaccumulative and very ecotoxic), and vP (very persistent, low hazards in the other endpoints). The dashed line denotes the classification threshold of $f = 0.17$, below which a hazard combination is classified as "regrettable".

In order to enable practitioners to use MCDA-ACA+P as well, it is also implemented in the SI-3 (under ´´MCDA-ACA+P - forUsers").

Discussion

MCDA method parameters

MCDA is a method that has been recommended for use in REACH Authorizations and Restrictions.[27] However, the precise method parameters most appropriate for chemical as-

sessment of alternatives have not been extensively discussed. In response to this need, we here investigate and recommend MCDA method parameters for the assessment of chemical alternatives, specifically objective hierarchies, aggregation, curvature of the value functions, weights, and the introduction of a classification threshold. Prior to this paper, to our knowledge, all MCDA-MAVT parameters found in the literature for the assessment of chemical alternatives were the default method parameters of a simple objective hierarchy, equal weighting, additive aggregation, and linear value functions. In the context of the assessment of chemical alternatives, these parameters would not be recommended, as the underlying decision logic cannot reproduce hazard assessment according to Article 57 of REACH. This is shown in London et al.[7] For the exact alignment with Article 57 of REACH, we recommend to use the parameters of MimicREACH; in a broader context, we propose to use MCDA-ACA as MCDA-ACA covers more objectives. Specifically, also substances that are very persistent and very ecotoxic and substances that are very bioaccumulative and very ecotoxic are rated regrettable with MCDA-ACA, which is not the case for MimicREACH (and Article 57 of REACH). This means that the MCDA-ACA method is more stringent than Article 57 of REACH. Additionally, MCDA-ACA includes the higher-level objectives PMT_{eco}, PM, ODP and GWP, which are not included in MimicREACH.

The objectives currently defined in MCDA-ACA include with one exception (the physical hazard of flammability) all minimum hazard criteria that were defined by the OECD in 2021.[18] However, as MCDA-ACA is a flexible method, it can easily be adapted to include additional hazards, if required. The flexibility of MCDA-ACA is also a strength in contrast to previously used methods that are more rigid such as set decision trees as used in GreenScreen®.

In MCDA-ACA as well as in MimicREACH and MimicGreenScreen, the attributes used (e.g., the half-life in soil) are converted into discrete values (hazard levels of very high, high, moderate and low). This conversion results in a loss of granularity as there are no continuous

values anymore but just four hazard levels. In our opinion, however, the conversion into discrete values is important, if not unavoidable, for two reasons. First, different jurisdictions use different thresholds. Discrete values makes it easier to adapt the method to jurisdictions outside the EU. For example, Article 57 of REACH states that a substance is bioaccumulative if the BCF is ≥ 2000.[22] However, the BCF threshold for bioaccumulation in the US is ≥ 1000[28]. The thresholds can be easily changed with discrete values while it is more difficult to implement a new continuous value function where these thresholds are still met. Secondly, and maybe even more important, Article 57 of REACH is very specific on which hazard combinations are potential SVHCs (and therefore regrettable) and which ones not. Even with the discrete values, it was only just possible (and with the help of the scaling factors) to correctly assign the hazard combinations to regrettable and non-regrettable. It would be very difficult to guarantee that all hazard combinations are always correctly assigned when a continuous value function is used.

Uncertainties in the input data and missing data

Uncertainties in the substance-specific data entering the method have not been explicitly addressed yet in this work. One option would be to run the evaluation several times, each time varying one of the uncertain data points (e.g., the half-life of the chemical in water), while keeping all the other input data points constant. This can be done as a sensitivity analysis where each of the uncertain data points is varied by the same percentage. Alternatively, the lowest and highest realistic values for any uncertain data point might be used (bounding analysis).[29] This allows the user to estimate whether the data point within its bounds has a strong influence on the results or not. Future work could also incorporate data uncertainties qualitatively. For example, it would be possible to evaluate the quality of the input data on a standardised scale (e.g., 1 could be "no information available", 2 "data uncertain", 3 "data certain" and 4 "data very certain"). The uncertainty scores could then be aggregated for the lower-level objectives with a minimum aggregation, meaning that if e.g., in PBT_{eco},

P has an uncertainty score of 3, B a score of 1 and T_{eco} a score of 2, the overall score of PBT_{eco} would be 1.

Another critical point – as in all methods that evaluate chemical alternatives – is missing data on chemical attributes, i.e., hazardous properties. However, by using a minimum, rather than an additive aggregation, for the higher-level objectives, the availability of data for a higher-level objective that indicate that the alternative is a regrettable substitute is sufficient to classify this alternative. Missing data for other higher-level objectives do not influence this assessment. However, missing data do influence the assessment if the MCDA outcome is "not regrettable" because additional data on insufficiently characterized hazards may change the outcome to "regrettable". We recommend in those cases to use calculated and/or predicted attributes to fill the missing data points. When calculated or predicted attributes are used, a sensitivity analysis using these values is recommended. The SI-1 Section S6 gives guidance on which methods to use. Additional guidance can be found in OECD [18].

Safe and Sustainable by Design

MCDA is a decision-making support tool that can assist in the design of safe and sustainable chemicals. [14,30] Therefore, the MCDA-ACA method could be a relevant tool for stakeholders to achieve the objectives of the EU's Green New deal. Dias et al. [31] presented seven requisites underpinning an overall evaluation procedure for Safe and Sustainable by Design (see also SI-1 Section S5). MCDA-ACA fulfills most of these requisites. Specifically, the aggregation in MCDA-ACA does not allow for trade-offs between objectives and the higher-level objectives are associated with regulatory reference points that act as classification criteria, thus the assessment is absolute and not relative. MCDA-ACA does currently not take the data quality into account, something that might need to be addressed in the future. Given the flexibility of MCDA-ACA, it is also possible to include more higher-level objectives including those that are suggested in Caldeira et al. [32], such as explosiveness or flammability. MCDA-ACA can therefore also assist in the design of safe and sustainable chemicals.

Implications

Methods for assessing alternatives to hazardous chemicals in a comprehensive way are much needed and we hope that MCDA-ACA is a step forward in this direction. However, hazard assessment methods including MCDA-ACA should not be treated as black boxes. It is important to understand the way these methods work in order to be able to communicate the results. Being transparent about how the results were obtained is especially important in larger companies, trade organizations or governmental agencies[6]. It might also be necessary to include other objectives such as costs or performance in the MCDA methods and to consider not only chemical-by-chemical substitution but also functional substitution or substitution by a change of the system[1].

In any case, more should be done than just looking through certain lists (e.g., the Candidate List of Substances of Very High Concern for Authorisation[33]) to decide whether a substance is a non-regrettable alternative. As pointed out by Slunge et al.[2], the European Commission[34] estimated in 2006 that there were approximately 1,500 substances with known SVHC properties and committed to "having all relevant currently known Substances of Very High Concern (SVHCs) included in the Candidate List by 2020".[2,35] However, by June 2024 only 240 substance entries were included in the Candidate List, including around 450 substances, which shows that those lists are not sufficient to identify regrettable substitutes.

Acknowledgement

This work received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement 860665 (PERFORCE3 Innovative Training Network).

Supporting Information Available

The Supporting Information-1 includes definitions for some of the terms used in the article, the thresholds that we suggest to use with MCDA-ACA and MimicREACH, the reasons for including scaling factors, the deviation of the data classification threshold for MimicGreen-Screen, and the requisites laid down in Table 2 of Dias et al.[31]. The Supporting Information-2 is an MS Excel file and contains the calculations for the hypothetical substances dataset and the real substances dataset.

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