Modifying multi-criteria decision analysis for assessments of chemical alternatives

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Abstract

Effectual assessment of chemical alternatives is necessary to avoid "regrettable" substitution. In a preceding study, an analysis of seven assessment-of-alternatives (AoA) methods found that none of them is fully aligned with Article 57 of the European REACH regulation, indicating a need for a method better reflecting European regulations. This paper presents a modified multi-criteria decision analysis (MCDA) method for the assessment of chemical alternatives (MCDA-ACA). We investigate and recommend MCDA method parameters for the assessment of chemical alternatives, specifically scope of objectives considered, 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 MCDA-ACA 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 frameworks, GreenScreen® and Article 57 of REACH alone.

The results show that MCDA-ACA can easily be adapted to other jurisdictions as required.

Keywords

Multi-criteria decision analysis, assessment of alternatives, GreenScreen, Article 57 of REACH, regrettable substitution, substance of very high concern (SVHC), minimum aggregation, chemical hazard assessment

Synopsis

We propose parameters for a modified multi-criteria decision analysis method to effectively 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. 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.[2] 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.[3] identified literature gaps and a research agenda to advance the AoA field in the six components listed by Jacobs et al.[2] One of the research needs they identified was to develop decision-making methods and tools for use in private and regulatory contexts and, specifically, to adapt emerging and existing decision-making tools for the (aggregation and) weighting of different hazard data. The most recent article in this series (Bechu et al.[4]) analysed the progress in the research agenda and concluded that there has been progress also in the method and tool development in decision-making. However, it was also stated that further guidance on the use of formal decision-making tools such as MCDA for alternative assessment is needed.[4,5]

In the accompanying paper by London et al. (2024), 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).[6] 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. The results of our analysis showed that none of the investigated alternative assessment methods use the same criteria as described in Article 57 of REACH. This also applies to Multi-Criteria Decision Analysis (MCDA), irrespective of how the parameters were selected. It was concluded that it might be possible to use MCDA if the condition of non-redundant objectives is not respected as this was the main reason why the decision logic in Article 57 of REACH could not be reproduced.

Other attempts to apply MCDA to decision making in assessments of chemical alterna-

tives have also been presented recently.[7–11] However, these studies did not justify the method parameters applied, nor was the variability of the results upon applying different method parameters investigated. 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 hazards criteria used in Article 57 of REACH (e.g., very persistent and very bioaccumulative).

Here we propose a modified MCDA method for the assessment of chemical alternatives, the MCDA-ACA method. The method deviates from a typical MCDA as it also allows redundancy in the parameters, which makes it possible to include combinations of hazards where a few lower-level objectives are included in more than one higher-level objective. The MCDA-ACA method also allows for the integration of various objectives, including (low) Global Warming Potential (GWP) and (low) Ozone Depletion Potential (ODP), and combines the objectives so that poor performance in one of the 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 new MCDA-ACA method is first presented and afterwards applied to two sets of hypothetical and real substances. 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.

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. One aim is also that the new method can rank the non-regrettable substances according to their hazard. The objectives included are:

- low Global Warming Potential (GWP), in order to avoid substances that are potent greenhouse gases
- low Ozone Depletion Potential (ODP), to avoid substances that can destroy the ozone layer
- low PBT_{eco} and low PB, to avoid persistent (P), bioaccumulative (B) and ecotoxic (T_{eco}) as well as very persistent and very bioaccumulative substances, in line with the criteria of Article 57 of REACH
- low 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
- low PMT_{eco} and low PM, to avoid persistent, mobile (M), and ecotoxic as well as very persistent and very mobile substances in line with the current CLP regulation
- low BT_{eco}, to avoid very bioaccumulative and very ecotoxic substances, in line with the criteria of GreenScreen® for substances that are GreenScreen Benchmark 1 (highest hazard level)
- low 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)

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.

According to the analysis by London et al.[6], a method based on MCDA seemed most effectual due to its flexibility and the possibility to explicitly set parameters. The five MCDA

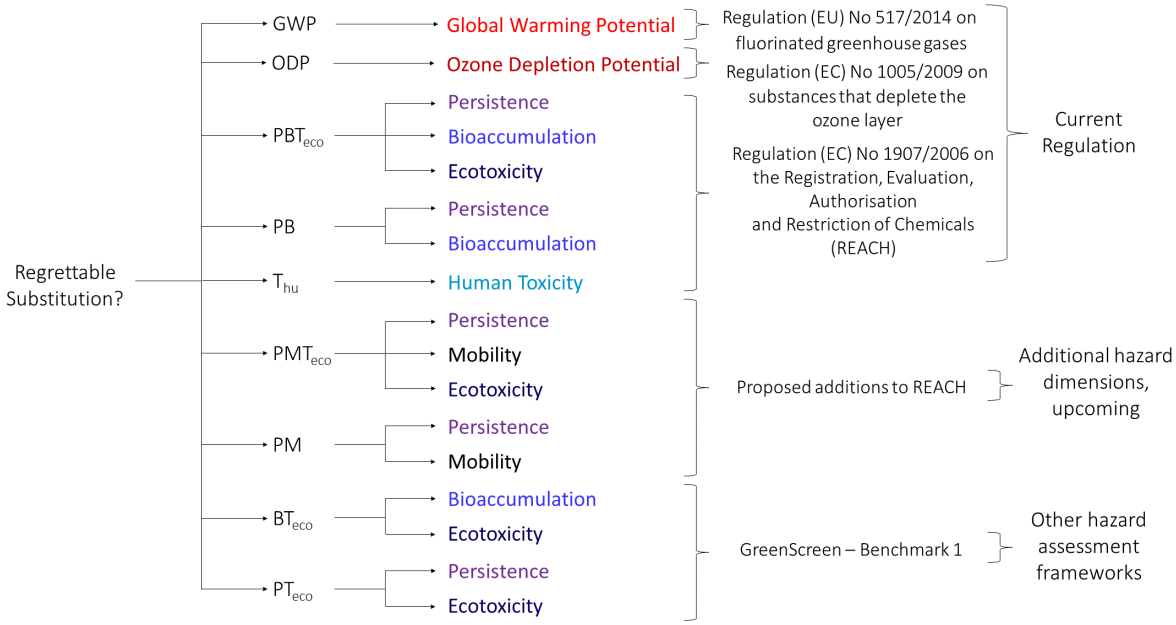

Figure 1: Objective hierarchy of the MCDA-ACA method. GWP and ODP are higher-level objectives that consist of three letters whereas P, B, M, T_{eco}, and T_{hu} are all individual lower-level objectives that are aggregated into various higher-level objectives. The different colors show the different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

parameters that can be varied and are investigated here are the objectives of the assessment (i) (e.g., low persistence), the attributes by which these objectives are measured (e.g., half-live in fresh water), the value function (with linear/non-linear curvature) 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). Provided in the SI-1, Section S1, are definitions of the terms objective (including objective hierarchy, higher-level objective, and lower-level objectives), attributes, value function (including curvature of value function), aggregation, and weights. Although MCDA objectives are usually directional (e.g., "low persistence" instead of just "persistence"), in this paper, the directionality of objectives is generally not indicated explicitly. This simplification is permissible, as for this MCDA all objectives are chemical hazards and so have the same desired directionality – low hazard is desired, high hazard is not. More information on the different types of curvatures and aggregation, and how curvature, aggregation and weighting influence the final hazard score in MCDA is provided by London et al. [6].

Datasets

The MCDA-ACA method was tested on two datasets: a hypothetical substances dataset and a previously published set of real substances. The hypothetical substances dataset contains 256 combinations of four hazards (persistence (P), bioaccumulation (B), human toxicity (T_{hu}), and ecotoxicity (T_{eco})) and four qualitative hazard levels (very high, high, moderate, and low). With the hypothetical substances, the steps 3) to 5) – data conversion, data aggregation and data classification – will be tested. For the hypothetical substances, the lower-level objectives of P, B, T_{eco}, and (T_{hu}) were categorized as very high (v), high (h), moderate (m), and low (l). For all hypothetical chemicals, the different hazard combinations were labeled manually as if they were classified according to the regulations shown in Fig. 1. 148 of the 256 substances have SVHC characteristics.

The real substance dataset was derived from an MCDA study by Zheng et al., who investigated 16 alternative substances to the flame retardant, decaBDE.[8] 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.[8] in the data gathering step. However, the data normalization was not adopted from Zheng et al.[8], but carried out by us using the thresholds from the Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment.[12] The normalized data were then used to investigate 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 conver-

sion, 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 persistent assessment of HFPO-DA.

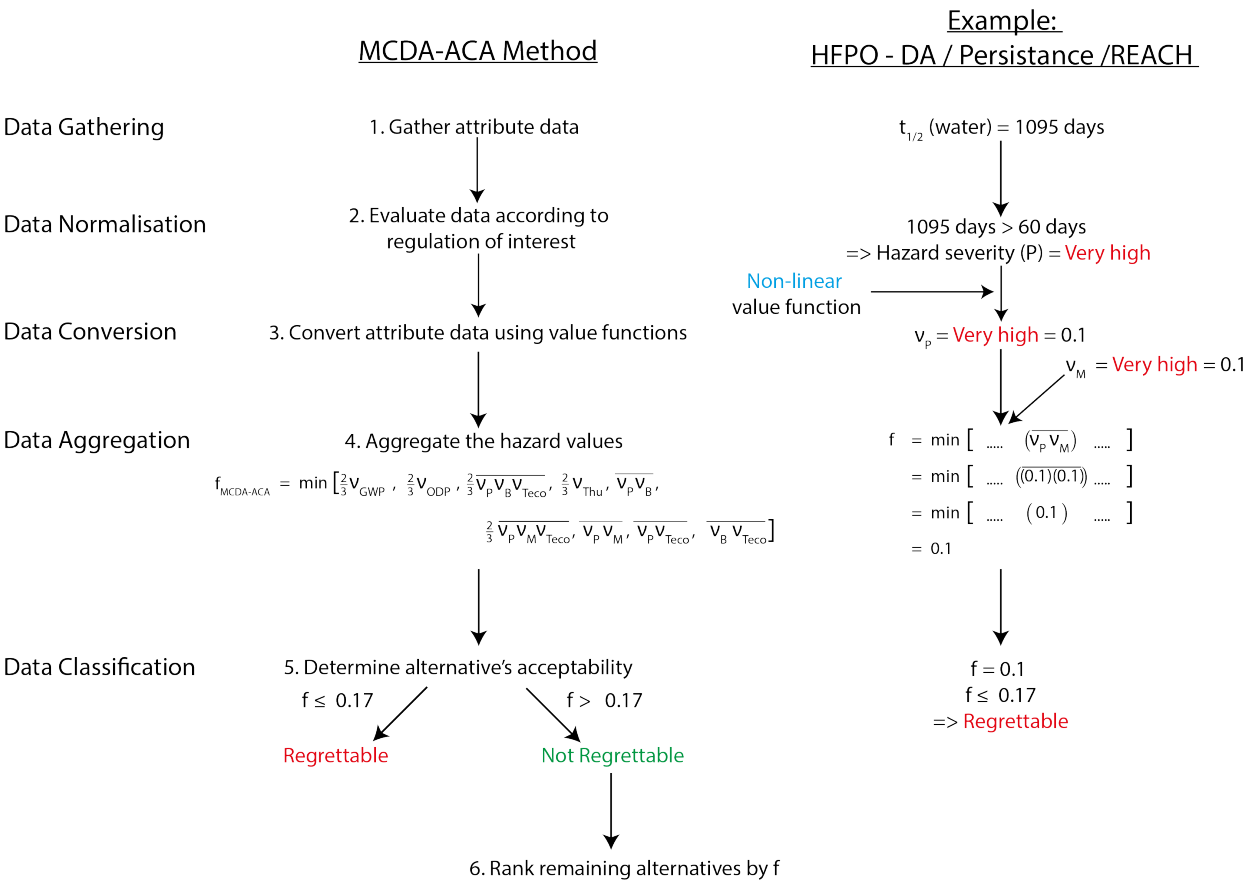

Figure 2: Flowchart showing the MCDA-ACA method. The flow chart on the left shows the general steps, the flow chart on the right the steps for the persistence assessment of HFPO-DA. The notation $\overline{X, Y}$ stands for the arithmetic mean of X and Y.

Data gathering. Attribute data need to be collected for the lower-level objectives of 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.[13]

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". For the use of the MCDA-ACA method in the context of European regulation, the thresholds from Annex XIII of REACH[14] can be used for P, B, T_{eco}, and T_{hu}. 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. For the assessment of M, the thresholds from the Commission Delegated Regulation (EU) 2023/707 (ref[15]) might be used. More details on the recommended thresholds, also those for GWP and ODP is provided in SI-1 Section S2. 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 "low 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 affect the MCDA output, f. This was one of the problems in using MCDA to reproduce the criteria of Article 57 of REACH, as some of the lower-level objectives (such as P) appear several times in the higher-level objectives.[6] As only one of the higher-level objectives determines the end result if minimum aggregation is used, the redundancy is no longer a problem.

Data classification. The MCDA output, f, is then used to classify the alternatives in terms of its 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:

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

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. 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. Table 1 shows examples of hazard combinations for each of the nine higher-level objectives identified in Fig. 1 that lead to "regrettable" or "non-regrettable" as outcomes.

The highest score for the regrettable hazard combinations obtained is 0.167, the lowest score for the non-regrettable hazard combinations 0.175. A classification threshold of 0.170

can therefore separate regrettable and non-regrettable hazard combinations. The scaling factor of 2/3 is needed because in some cases the value function chosen here leads to hazard scores above 0.17, but the REACH regulation requires the outcome "regrettable", for example for high P, high B and high T_{eco}. SI-1 Section S3 explains for each higher-level objective in detail why the scaling factor is needed. 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. A non-linear (convex) value function is necessary as it would otherwise not be possible to classify cases such as high P, high B and high T_{eco} as regrettable and at the same time very high P, high B and medium T_{eco} as non-regrettable. With a linear value function, both examples would receive the same score, while a convex value function can separate them (the first example receives a lower score than the second one).

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	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 modified 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®.[16]

As a first step, objective hierarchies were created using the lower-level objectives identified in Article 57 of REACH[14] and in Annex 3 of GreenScreen®.[16] Secondly, an aggregation equation was created for both models. Finally, the data classification step was carried out to replicate the original frameworks.

Results

Applying the MCDA-ACA method

To test the MCDA-ACA method, it was applied to the 256 hypothetical substances. For each substance f was determined, and the substances were ranked by descending f. Of the 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 (vP, lower-level, $f = 0.47$) is classified as "not regrettable", whilst Substance 253 ($\mathrm{vT_{hu}}$, 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."

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 correctly identifies all 148 SVHCs.

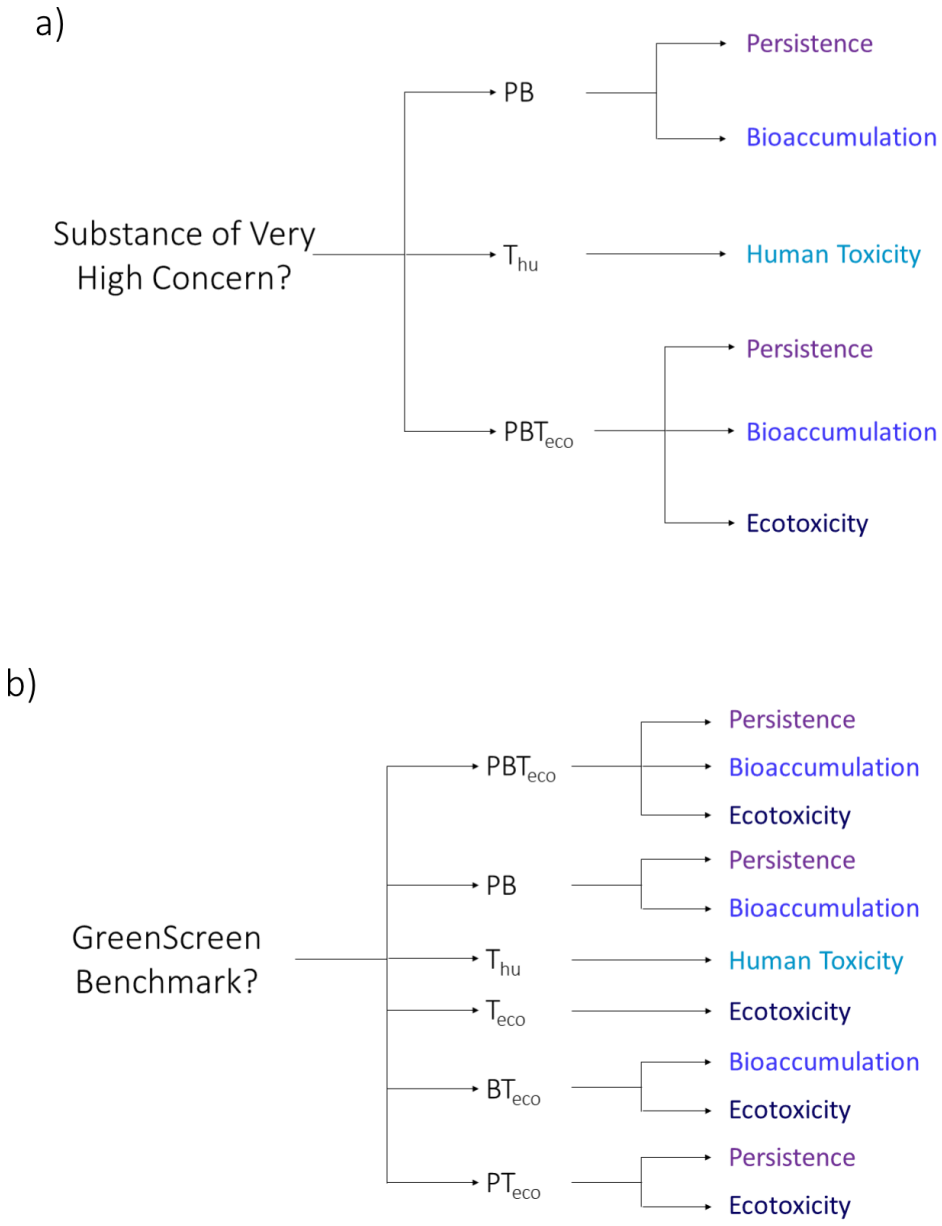

Figure 3: Objective hierarchy of a) MimicREACH and b) MimicGreenScreen. The different colours show the different lower-level objectives.

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}, GWP and ODP are not included as higher-level objectives in MimicGreenScreen. 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.

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

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)

- Four specific cases where GreenScreen® and the MCDA decision logic assign Benchmarks 2 instead of 3 and vice versa (rows 5 to 8 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
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

Discussion

MCDA is a method that has been recommended for use in REACH Authorizations and Restrictions.[17] However, the precise method parameters most appropriate for chemical assessment 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 scope, aggregation, curvature of the value functions, weights, and the introduction of a classification threshold. Prior to this paper, to our knowledge, all MCDA-MAUT method parameters found in the literature for the assessment of chemical alternatives were the default method parameters of a simple objective hierarchy, namely 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 our accompanying article London et al.[6] For the exact alignment

with Article 57 of REACH, we recommend to use the method parameters of MimicREACH; in a broader context, we propose to use MCDA-ACA as MCDA-ACA covers more objectives.

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®.

Uncertainties in the data entering the method have not been explicitly addressed yet in this work. Future work using the method presented here could however incorporate data uncertainties. For example, it would be possible to evaluate the quality of the input data on a standardised scale. As the result of the minimum aggregation ultimately only depends on one of the higher-level objectives, the uncertainty evaluation could be easily transferred to the final result. 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". Guidance on the data source hierarchy for chemical hazard information is provided in OECD[18].

In our paper, the MCDA-ACA method is described as a modified MCDA (MAUT) method. In an MCDA there should be no redundancy in the objectives hierarchy; the objectives chosen should be independent of one another,[17] and ideally the number of lowest-

level objectives should be smaller than 15.[19] These conditions are not fully met by the MCDA-ACA method. The objectives may not be independent of one another, for example there is some correlation between persistence and bioaccumulation,[20] and global warming potential is a function inter alia of persistence in air. However, persistence, bioaccumulation and GWP are the endpoints that are used to evaluate chemical alternatives in EU regulations. We decided therefore to accept that they are not completely independent of each other. There is also redundancy in the scope of objectives considered with some lower-level objectives appearing several times. The risk of double counting is, however, mitigated by using a minimum aggregation for the higher-level objectives, as described before.

Persistence appears several times in the scope, and a question here is whether the MCDA-ACA method should include persistence alone ("P-sufficient") as one of the higher-level objectives. One of the possible scopes investigated included this P-sufficient approach (see SI – mimicGreenScreen + P). However, whilst regulatory thresholds already exist for the other hazard combinations, thresholds for a P-sufficient approach do not yet exist, i.e., at what half-life is persistence alone sufficient for a substance to be considered a regrettable substitute? However, deciding at what point persistence in the absence of other hazards is severe enough for an alternative to be considered a regrettable substitute is outside the scope of this paper. For this reason, persistence alone was not included in the objective hierarchy of the MCDA-ACA method, however it can be used in the alternative classification step as a secondary hazard that can be used to differentiate between non-regrettable alternatives.

MCDA is a decision making method that can assist in the design of safe and sustainable chemicals.[11,21] 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.[22] presented seven requisites underpinning an overall evaluation procedure for Safe and Sustainable by Design (see also SI-1 Section S4). 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.[23], such as explosiveness or flammability. MCDA-ACA can therefore in our point of view also assist in the design of safe and sustainable chemicals.

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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 MimicGreenScreen and the requisites laid down in Table 2 of Dias et al.[22]. The Supporting Information-2 is an excel file and contains the calculations for the hypothetical substances dataset and the real substances dataset.

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