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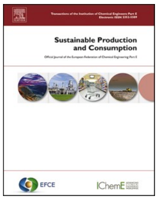

A composite indicator for evaluating safety and sustainability by design and circularity in emerging technologies

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ABSTRACT

The application of the Safe-and-Sustainable-by-Design (SSbD) framework to emerging technologies (i.e. chemicals, bio-based products and other related materials manufacturing processes) faces significant challenges due to the limited data availability of these processes and because their level of optimization and implementation is less developed compared to traditional production models. However, the transition to the circular economy must be based on safer, more efficient and sustainable production models. In this research article, a robust methodology that accurately assesses the sustainable and circular potential of these processes is developed. This methodology proposes a new composite indicator (CI-SSbDC) based on the European Commission SSbD (EC-SSbD) framework guidelines. CI-SSbDC assesses safety, sustainability and circularity, and can be applied to bio-based and fossil-based products and technologies. The CI-SSbDC indicator ranges from 0.01 to 1, where "0.01" indicates the least promising option and "1" the most promising one. To examine how different levels of compensation influence the composite indicator value, several aggregation methods were used, including additive, geometric and harmonic means. The composite indicator was applied to three production variants for the same product, to demonstrate its effectiveness and potential, including also sensitivity analysis to test the influence of the assumptions made in the methodology. Despite the ongoing development of the EC-SSbD framework, the proposed composite indicator serves as a practical initial approach to put it into practice, integrating the critical circularity pillar essential for the bioeconomy and aligning with waste management strategies and life cycle analysis methodologies. Also, it could serve as a first guide to highlight where to focus efforts on for an effective implementation of SSbD and circularity frameworks.

Acronyms and symbols

Acronyms

CI-SSbDC	Composite Indicator – Safe and Sustainable by Design and Circularity
EC-SSbD	European Commission Safe and Sustainable by Design framework
LCA	Life Cycle Assessment
MCDA	Multiple Criteria Decision Analysis
SSbD	Safe and Sustainable by Design

Equation symbols

AC	Acidification
CC	Climate change
CD	Circular dimension
CD_{CRM}	Critical raw materials
CD_{EF}	E-factor
CD_{MI}	Material index
CD_{REC}	Recyclability
CD_{RM}	Renewable materials
CD_{RR}	Recirculation Rate
CD_{WL}	Waste to landfill
EcD	Economic dimension
ED	Environmental dimension
ET	Ecotoxicity

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(*continued*)

EUM	Eutrophication marine
EUT	Eutrophication terrestrial
HD	Hazards dimension
HeD	Health dimension
HNTC	Human toxicity non-carcinogenic
HTC	Human toxicity carcinogenic
IR	Ionizing radiation
LU	Land use
MSP	Minimum selling price
NPV	Net present value
OD	Ozone depletion
PM	Particular matter
POF	Photochemical ozone formation
PP	Payback
RF	Resources, fossil
RM	Resources, mineral
w	Weighting factor
WU	Water use

1. Introduction

The Safe-and-Sustainable-by-Design framework of the European Commission (hereafter, the EC-SSbD framework) was introduced in 2022 to stimulate the safe and sustainable life-cycle-based development of chemicals and materials (Caldeira et al., 2022a, 2022b). The framework was disclosed in a European Commission recommendation in 2022/2510 and related methodological guidance as well as its application to several case studies have also been recently published (Abbate et al., 2024; Caldeira et al., 2023).

The EC-SSbD framework advocates for safer and more sustainable production processes and products from the early stages of design, with the aim of promoting more sustainable value chains in the production and consumption sectors. SSbD could be seen as a practical tool and methodology to achieve the aims outlined in the Sustainable Development Goal (SDG) 12 (Responsible Consumption and Production). Although SDG12 and SSbD approach sustainability from slightly different angles, there are some synergies and linkages between them. SDG12 focuses on resource efficiency to avoid their depletion, and SSbD could contribute as it ensures that products are designed to be efficient and produce less waste, also promoting the recyclability of resources and their sustainable use. In this aspect, the circular economy could also be promoted, as enhancing resource efficiency and reducing waste are two of the main aspects to be framed when thinking about moving from a linear production model to a circular one. SDG12 also aims at minimizing the environmental burden of products and services within a life-cycle thinking approach, which is also in line with the SSbD framework, as it encourages considering the environmental impact of products throughout their life cycle from an early design phase. One of the objectives of SDG12 is also to encourage industries to adopt sustainable practices and be certified, with a view to corporate responsibility, and the implementation of the SSbD framework and practices drives companies to be safer and more sustainable, and thus more responsible in the production processes, since the design phase.

In order to assess a production process, product, technology or service under the EC-SSbD framework, multiple steps are required to be evaluated, including hazards, risks and sustainability implications of chemicals and materials, throughout their entire life cycle, by innovators working in the research and innovation areas, assessors taking care of sustainability and circularity approaches of production processes and products, known as “practitioners”. This framework also encourages the integration of circularity in product development to discourage linear value chains. European Commission Recommendation (EU) 2022/2510 identifies four steps, namely the assessment of (i) hazardous properties of chemicals, (ii) human health and safety aspects in production and processing, (iii) environmental and human health risks in the use phase, and (iv) environmental impacts throughout the entire life cycle. An optional phase not formally included in the framework, but is advised, is the assessment of socioeconomic sustainability along the whole life cycle (Abbate et al., 2024).

Each step of the EC-SSbD framework involves the use of indicators to assess the potential impact/risks that the chemical or material of concern may have. Nevertheless, this set of indicators should provide a comprehensive and complete information, being aware that the performance of a production process or product may be good for some indicators and worse for others. The analyst and decision-makers must face a decision-making dilemma of assessing whether or not the material or chemical of interest performs well from a safety and sustainability standpoint. This context of decision making in a multi-criteria environment is not uncommon when policy and ‘decision makers’ must use the results of a variety of sustainability methods to evaluate complex systems (Campos-Guzmán et al., 2019). To aid in the interpretation of all this information, Multi-Criteria Decision Analysis (MCDA) has been proposed as very promising (Dias et al., 2024). MCDA is a methodology that has been developed to deal with decision-making problems with a finite set of alternatives, assessed according to a pool of indicators selected from the existing literature and database, as well as via interaction with relevant stakeholders (Greco et al., 2016). The use of multiple indicators in decision-making analysis is thought to be beneficial compared to individual indicators, as those could provide a more holistic perspective, reducing the risk of misinterpretation and offering a more robust framework. It is important to highlight that the issue with single indicators is that the human brain cannot pay attention to more some items at the same time. There is research that explored this topic and shows that humans can focus only on a limited number of pieces of information at the same time (Ma et al., 2014; Paas et al., 2003). Consequently, the use of composite indicators can enable accounting for all the selected information (e.g., indicators) in a fair manner at the same time.

This methodology is capable of handling different types of challenges that are recurrent in SSbD-driven projects (Hristozov et al., 2023; Dias et al., 2024):

1. Work with indicators with different measurement scales, including quantitative and qualitative, as well as deterministic and uncertain;
2. Support tiered assessments, from low TRL and data-scarce environments to high TRL and data-rich environments;
3. Include the preferences of the stakeholders in relation to the trade-offs that can be accepted between the indicators;
4. Aggregate safety, sustainability and functionality indicators, as well as include stakeholders' preferences, to provide different types of decision recommendations. These recommendations can be a ranking of alternatives from best to worst, sorting alternatives into classes with a preference order, choosing of a subset of suitable alternatives, and clustering those that share similar performances.

MCDA methods have already been used to integrate some safety and sustainability concepts in the assessment of materials and chemicals, well before the EC-SSbD framework was proposed (Lindfors, 2021; Thies et al., 2019; Zanghelini et al., 2018). However, a recent review that specifically analyzed the use of MCDA methods that combine safety and sustainability found that only 27 of the 110 reports reviewed considered both (Dias et al., 2024). Out of this 27, most of the studies used MCDA methods that can only perform comparative assessments, where it is necessary to have at least two (or sometimes three) alternatives to be compared to make the assessment possible. In addition, all the studies except two used MCDA methods that assume full compensation between the indicators, meaning that the indicators where the performance is good can compensate for the indicators where the performance is bad. What is more, none of the 27 studies included circularity indicators in their assessment. While these 27 studies show a promising stream of research to use MCDA methods to include safety and sustainability, there are currently no SSbD-based solutions using MCDA where it is

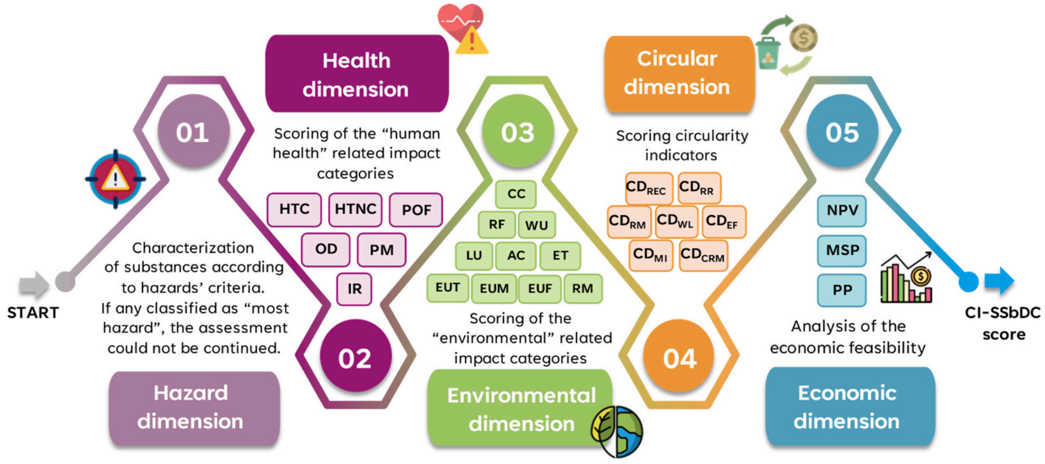

Fig. 1. Dimensions and indicators considered for calculating the CI-SSbDC score. Acronyms: HTC (human toxicity carcinogenic), HTNC (human toxicity non carcinogenic), POF (photochemical ozone formation), OD (ozone depletion), PM (particular matter), IR (ionizing radiation), CC (climate change), ET (ecotoxicity), AC (acidification), RM (resources, mineral), WU (water use), RF (resources fossil), LU (land use), EUM (eutrophication marine), EUT (eutrophication terrestrial), CD_{REC} (recyclability), CD_{RR} (recirculation rate), CD_{RM} (renewable materials), CD_{WL} (waste to landfill), CD_{EF} (E-factor), CD_{MI} (material index), CD_{CRM} (critical raw materials). NPV (net present value), MSP (minimum selling price), PP (payback).

possible, at the same time, to (i) apply it with only one alternative, as well as more than one, (ii) test the effect of different compensation levels on the final decision recommendation, and (iii) include circularity indicators in addition to safety and sustainability ones.

Overall, MCDA methods show remarkable potential to aid the interpretation of the results of the EC-SSbD framework steps and streamline the decision-making process for responsible innovation. Based on these advances in the literature, our work proposes the use of MCDA methods to develop a composite indicator to comprehensively assess the safety, sustainability and circularity of products.

The composite indicator is called CI-SSbDC (Safe-and-Sustainable-by-Design and Circularity). CI-SSbDC aims to effectively support process developers to evaluate the potential of new technologies and processes following the EC recommendations proposed under the safe, sustainable, and circular perspectives from an early stage of development, that is processes at low-Technology Readiness Level (TRL). Its application is demonstrated for one bio-based product with three production processes, showing the contribution of the composite indicator on the assessment of trade-offs between the different pillars of sustainability as well as circularity. The manuscript is structured in three main sections: Section 2 introduces the methodology; Section 3 delves into the application of the CI-SSbDC in three case studies for validation and Section 4 comprises sensitivity analysis for those parameters pre-set at a given value to analyze the methodological robustness.

2. Methodology

In this section, we detail the process used to build and test, with three proposed case studies (Section 2.3), the CI-SSbDC, which can be used to assess one or more production processes based on the combination of hazard, sustainability, and circularity approaches. The model was shaped through an MCDA process that included three stages. First, we selected the parameters against which the alternatives can be evaluated, i.e., indicators. Second, a preference model was built to define how the performances on each indicator influence the final CI. In addition, during this second stage, aggregation algorithms were chosen to provide the final decision recommendation, which in this case is a single score. Third, we tested the CI-SSbDC in three case studies. The following sections describe these steps for the development and testing of CI-SSbDC in detail.

2.1. Indicators used in the Composite Indicator – Safe and Sustainable by Design and Circularity (CI-SSbDC)

The indicators used for the development of the CI-SSbDC are hierarchically structured in five dimensions, namely "hazard dimension" (HD), "health dimension" (HeD), "environmental dimension" (ED), "circular dimension" (CD), and "economic dimension" (EcD) (Fig. 1). The choice of these five dimensions was based on the current structure of the SSbD framework proposed by the European Commission (Abbate et al., 2024; Caldeira et al., 2022a, 2022b), the European Bioeconomy Action Plan (European Commission, 2018), as well as of the European Green Deal (European Commission, 2021a, 2021b). In all these initiatives, sustainability, circularity and clean innovation strategies are key aspects to be fulfilled.

2.1.1. Hazard dimension (HD)

The hazard dimension is assessed by considering the potential hazards that a technology or production process could entail given the use of particular chemicals. This dimension should be evaluated for all input materials required in the production process and/or technology. Each of the inputs should be categorized following the guidelines available in the technical report "Safe and Sustainable by Design: chemicals and materials" developed by the Joint Research Center of the European Commission (Caldeira et al., 2022a, 2022b), summarized in Table 1.

To know whether an input material is classified as "most harmful", "substance of concern" or "other hazard properties", the analyst should use safety data sheets or substance databases related to the hazard properties, such as OpenFoodTox (Carnesecchi et al., 2023), Hazardous Substances Data Bank (HSDB®) (US National Library of Medicine, 2024) or Occupational Chemical Database (OSHA, 2024), among others.

Following the indication of Abbate and co-authors (Abbate et al., 2024) and Caldeira and co-authors (Caldeira et al., 2022a, 2022b), we consider this dimension as a cut-off criterion, which means that, if any of the input materials required in the production process or technology is categorized as "most harmful", then the calculation of the CI-SSbDC composite indicator cannot be continued.

2.1.2. Health dimension (HeD)

Most emerging products and processes do not have a comprehensive database on the health aspects that their use could entail (Yadav et al., 2021). With this in mind, to score the health dimension HeD, we consider the environmental life cycle assessment impact categories

Table 1
Categorization of substances according to hazard dimension. Identification of properties and possible hazards.

Type of hazards	Human health	Environmental	Physical
Most harmful substances	Carcinogenic Cat. 1A and 1B Germ cell mutagenicity Cat. 1A and 1B Reproductive or developmental toxicity Cat. 1A and 1B	Persistent, bioaccumulative and toxic or very persistent and very bioaccumulative	–
	Endocrine disruption Cat. 1 Respiratory sensitisation Cat. 1	Persistent, mobile and toxic/very persistent and mobile	
	Specific target organ toxicity, repeated exposure Cat 1.	Endocrine disruption Cat. 1	
Substances of concern	Skin sensitisation Cat. 1 Carcinogenic Cat. 2	Hazardous for the ozone layer	–
	Germ cell mutagenicity Cat. 2 Reproductive or developmental toxicity Cat. 2 Specific target organ toxicity, single exposure Cat 1 and 2	Chronic environmental toxicity (chronic aquatic toxicity)	
	Specific target organ toxicity, repeated exposure, Cat 2 Endocrine disruption Cat. 2	Endocrine disruption Cat. 2 (environment)	
Other hazards properties	Acute toxicity Skin corrosion and/or irritation	Acute environmental toxicity (acute aquatic toxicity)	Explosives, flammable gases, liquids and solids Aerosols
	Serious eye damage or eye irritation		Oxidizing gases, liquids, solids Gases under pressure
	Aspiration hazard Cat. 1		Self-reactive Pyrophoric liquids, solid
	Specific target organ toxicity, single exposure Cat 3		Self-heating In contact with water emits flammable gases
	Specific target organ toxicity, single exposure Cat 3		Organic peroxides Corrosivity Desensitised explosives

related to health damage potential (Zappe et al., 2020; Kobayashi et al., 2015a, 2015b). This consideration is also supported by the PARC SSbD Toolbox version 0.1 Guidebook (2024), in which the damage at the end of the cause-effect chain (in this case, health damage) is estimated by correlating the mid-point impact categories and their damage potentials. To this end, considering the impact categories affecting health damage should be an appropriate procedure.

For this purpose, the following impact categories and related impact scores are evaluated under the HeD scope: human toxicity carcinogenic (HTC), human toxicity non-carcinogenic (HTNC), ionization radiation (IR), photochemical ozone formation (POF), particular matter (PM), and ozone depletion (OD). All the impact categories belong to the "human health" damage category of the ReCiPe EndPoint methodology (Huijbregts et al., 2017).

Table 2
Circularity indicators considered for assessing the circular dimension. Acronyms: CD_{MI} (circularity indicator – material intensity index), CD_{CRM} (circularity indicator – critical raw materials), CD_{RM} (circularity indicator – renewable materials), CD_{EF} (circularity indicator – E-factor), CD_{WL} (circularity indicator – waste to landfill), CD_{REC} (circularity indicator – recyclability), CD_{RR} (circularity indicator – recirculation rate).

Acronym	Indicator	Definition	Equation
CD_{MI}	Material intensity index (kg/kg)	Amount of raw materials per product produced	$CD_{MI} = \frac{kg\ of\ inputs}{kg\ product}$
CD_{CRM}	Critical raw materials presence	Use of materials present in the list of critical materials	No equation required, only report if critical material(s) present or not.
CD_{RM}	Use of renewable materials	Amount of renewable feedstock/energy per total amount of inputs	$CD_{RM} = \frac{amount\ of\ renewable}{total\ inputs}$
CD_{EF}	E-factor	Ratio between mass of waste per mass of input chemical/materials	$CD_{EF} = \frac{kg\ of\ waste}{kg\ input}$
CD_{WL}	Amount of waste to landfill	Amount of waste disposed in landfill per kg of total outputs	$CD_{WL} = \frac{kg\ waste\ to\ landfill}{kg\ outputs}$
CD_{REC}	Recyclability	Is/are the product/products obtained recyclable?	No equation required, only report if the product/s are recyclable or not.
CD_{RR}	Recirculation rate	Amount of recirculated material/chemical in the production process	$CD_{RR} = \frac{kg\ material\ recirculated}{kg\ inputs}$

2.1.3. *Environmental dimension (ED)*

The environmental dimension is assessed taking into account all impact categories associated with the environmental product footprint (PEF) method, as recommended in the SSbD guidelines and in the ILCD handbook (European Commission, 2021a, 2021b). Impact categories that were already included in the "health dimension" dimension were excluded to avoid double-counting between CI dimensions. As a result, climate change (CC), eutrophication-terrestrial (EUT), eutrophication-freshwater (EUF), eutrophication-marine (EUM), ecotoxicity (ET), acidification (AC), resources-mineral (RM), resources-fossil (RF), land use (LU), and water use (WU), were included.

2.1.4. *Circularity dimension (CD)*

Quantitative and qualitative indicators were used to evaluate the circularity dimension. Their selection was made according to the EC-SSbD guidelines. A total of seven indicators were identified, of which five are quantitative and two are qualitative. Table 2 includes all the indicators of the circularity dimension, their acronyms, definitions and equations used for all calculations.

For the selection of the above, *firstly*, circularity indicators were selected from the EC-SSbD annex guidelines, bearing in mind that this selection has been made according to (1) easiness for data gathering to calculate the indicators, (2) easiness for quantifying the indicators and (3) adequate indicators to effectively and comprehensively evaluate the circularity potential. *Secondly*, to ensure that the selected indicators are quite commonly used in the literature, a literature review was performed to evaluate how the selection made compares to the circularity assessments research trends. For this purpose, a total of 183 articles were evaluated in a targeted review. The analysis and related assumptions are available in Supplementary material Table SM1 and Fig. SM1.

As a result of our review, we selected the most commonly used indicators. More specifically, CD_{MI} was used in 17 reports, CD_{CRM} in 20, CD_{RM} in 9, CD_{EF} in 30, CD_{WL} in 44, CD_{REC} in 32, and CD_{RR} in 41.

2.1.5. Economic dimension (EcD)

The economic dimension is measured by considering the most recognized financial metrics to assess whether a process under analysis is feasible and economically viable or not (Ioannidou et al., 2023; Pan et al., 2023; Rajendran et al., 2023). We considered the net present value (NPV) (Žižlavský, 2014), the minimum selling price (MSP) (Martinez-Hernandez et al., 2019), and the payback period (PP) (Kiran, 2022). The selection is based on a state-of-the-art review of the relevant literature from 2014 to 2024. Relevant information was collected from a total of 244 articles, of which 179 were suitable for analysis (see Supplementary material Table SM2). Within these articles, NPV was used in 79 reports, payback in 38 and MSP in 86.

2.2. Preference model

The preference model defines how information on the performance of alternatives and the decision-makers preferences are considered together to provide the target decision recommendation. The selection of the relevant MCDA method to provide such a recommendation is a specific process in itself, which should not be underestimated (Cinelli et al., 2022a; Wątróbski et al., 2019). Selecting an MCDA method that does not fit the problem at hand may lead to misleading decision recommendations (Cinelli et al., 2022b). As far as the requisites of the multiple criteria aggregation in the SSbD framework are concerned, a recent paper by Dias et al. (2024) provided initial guidelines. The authors stressed the need to keep in mind that indicators in SSbD-based assessment may have different measurement scales (qualitative and quantitative), and the desired outcome of the CI may be a grade level (e.g., class “A”, “B”, “C”) or a cardinal one (e.g., score of 36.5 on a scale from 0 to 100). These authors also point out that according to the type of input data and the desired decision recommendation, different MCDA methods are needed. According to these guidelines, and based on the formulation of our MCDA process, we used the MCDA method selection software (MCDA-MSS) (available free of charge at http://mcdamss.com) to aid in the MCDA methods selection.

The MCDA-MSS operates as a meta-decision support system, designed to guide users in selecting the most appropriate MCDA method (Cinelli et al., 2022a). MCDA-MSS uses a detailed taxonomy to characterize decision-making problems across several criteria, including problem formulation, preference elicitation, and desired decision recommendations. Users enter specific characteristics of their decision-making problem, and the software evaluates them against a library of more than 200 MCDA methods, analyzing compatibility based on the defined characteristics. This process helps identify a method that best aligns with the unique requirements of the study, thus optimizing the decision-making process. The MCDA-MSS considered here provided a set of suitable MCDA methods, as well as the set of choices with the MCDA-MSS (Supplementary material Fig. SM2). Key answers that affected the choice of the method include:

1. Obtain a complete classification through scoring. *Rationale*: CI should be applied to a single alternative or a group of alternatives to understand how well it performs on a scale and/or how much better or worse one alternative is compared to the other(s);
2. Use cardinal values to define performance for qualitative and quantitative indicators. *Rationale*: the performance of each alternative should be assigned a numerical value that defines its performance in relation to the respective dimension.
3. Use weights to differentiate the importance of indicators and dimensions. *Rationale*: the decision-maker should be able to choose which indicators and/or dimensions are more important than others during the aggregation stage.

Table 3
Aggregation equations considered for the assessment.

	Equation	Description
Additive weighted average	$\sum_{i=1}^{n} I_i \cdot w_i$	“*I*” represent the individual scores on each indicator and “*w*” the weight factor
Geometric weighted average	$\prod_{i=1}^{n} I_i^{w_i}$	
Harmonic weighted average	$1 \Big/ \sum_{i=1}^{n} \frac{w_i}{I_i}$	

4. The decision recommendation should be a single deterministic one. *Rationale*: Being the first version of the CI, the decision recommendation should be as simple as possible to understand for non-MCDA experts. More specifically, the intended users of the CI-SSbDC include process developers who are testing the performance of new processes for target products. The applicability of our CI focuses on low TRL levels, such as pilot scale.

The recommended method by the MCDA-MSS is the Multi-Attribute Value Theory (MAVT), an MCDA method introduced by Ralph Keeney and colleagues (Keeney, 2020; Keeney and Raiffa, 1976). MAVT builds upon the concept of value-focused thinking (Keeney, 2020), where the values of ‘decision makers’ are operationalized through different attributes, which in our CI are indicators. For each indicator, a (marginal) value function is defined. This translates the raw performance of the indicator (e.g., \$0.2/product) into a value score (e.g., 0.5 on a scale from 0 to 1, where 0 is the worst and 1 is the best score) that represents the degree to which a decision objective (e.g., minimizing product cost) is achieved (Bottero et al., 2014). In order to shape the value functions between 0 and 1 for each indicator, equations and graphical models

Table 4
Value functions: considerations and assumptions made per dimension. Acronyms: NPV: net present value, PP: payback period, MSP: minimum selling price, HD: hazard dimension, HeD: health dimension, CD: circularity dimension, ED: environmental dimension, EcD: economic dimension.

Dimension	Values assigned	Values assigned by
“Hazard” (HD)	Discrete Most harmful substances (stop the assessment), substances of concern (0.5), other hazards (1)	Research team
“Health” (HeD) and “Environmental” (ED)	Continuous 0.01 to 1, percentiles from 10th to 90th	Equations fitting the impact scores of 300 chemicals from the EcoInvent database
“Circularity” (CD) (2 qualitative: critical raw materials and recyclability)	Discrete A binary value function is applied for both indicators, where the lowest score (0.01) is applied if critical raw materials are present or if the resulting products are not recyclable. Otherwise, a score of 1 is used.	Research team
“Circularity” (CD) (5 quantitative)	Continuous Piece-wise linear on the whole range	Research team
“Economic” (EcD) – NPV, PP	Discrete 0.01: Negative NPV, PP longer than the useful life. 1: positive NPV, PP lower than the project lifetime.	Research team
“Economic” (EcD) – MSP	Continuous If the product market value is the same as the MSP obtained, then the value is 0.5, if not, linear function from 0.5 to 1	Research team

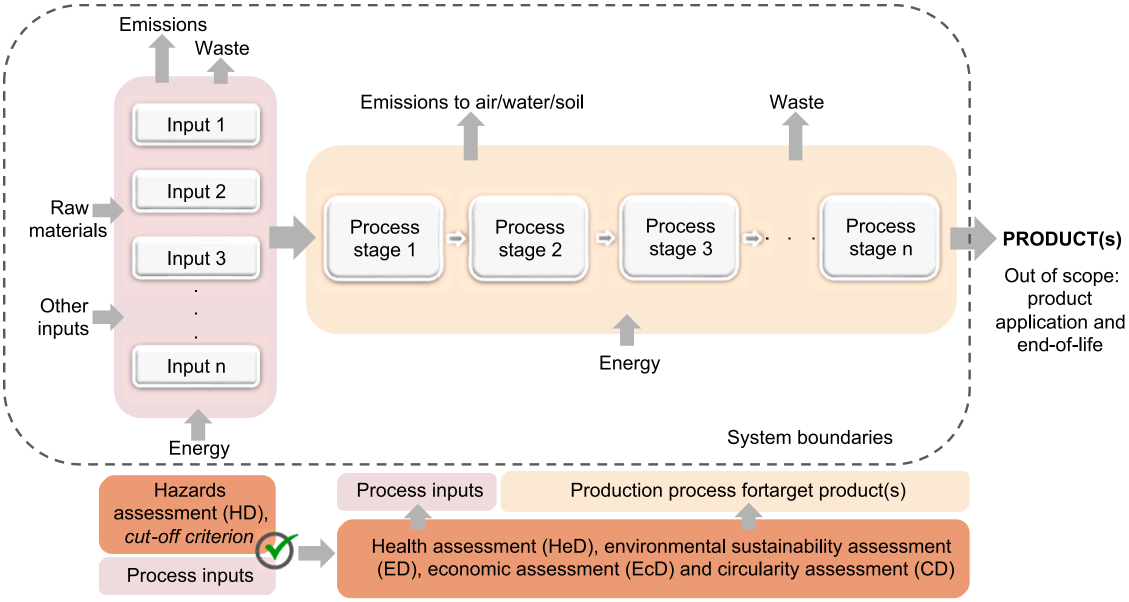

Fig. 2. Representation of the alignment between the life cycle and CI-SSbDC assessment steps and boundaries.

were developed, based on extensive data analysis. The following sections describe the methodological basis and assumptions of the value functions.

The last stage of the development of the preference model consisted of the selection of the aggregation algorithms to provide the final score of the alternative(s). In the EC-SSbD framework, the role of the different aggregation algorithms was analyzed to result in a final evaluation (Caldeira et al., 2022a, 2022b). The proposed framework also tested algorithms with lower degrees of compensation when applying the SSbD framework in case studies (Caldeira et al., 2023). However, the recent SSbD guidance does not define which aggregation algorithm to use (Abbate et al., 2024). In this context, we selected three aggregation algorithms for CI-SSbDC, as they resemble some possible aggregation preferences of different decision-makers. These include additive, geometric, and harmonic weighted averages (see Table 3). These aggregation functions allow accepting different levels of trade-offs between indicators and dimensions (Wilson and Wu, 2017; Langhans et al., 2014). The additive weighted mean assumes full compensation between indicators and dimensions, meaning that poor performance on one indicator or dimension can be compensated by good performance on one indicator or dimension. The geometric weighted average limits this level of compensation and is tailored to decision-makers who want to penalize any alternative that performs poor on even a single indicator or dimension. A similar reasoning applies to the harmonic weighted average, with the difference that the compensation accepted by this algorithm is even lower than that granted by the geometric one.

2.2.1. *Value functions development for the indicators of the Composite Indicator – Safe and Sustainable by Design and Circularity (CI-SSbDC)*

In this section, the approach used to develop the value functions for each indicator of the CI-SSbDC is presented. The value functions for the CI-SSbDC start from the worst performance with a score of 0.01, and increase (non-linearly) until the best performance with a score of 1.

The considerations and assumptions to shape the value functions are described in Table 4, combining expert-based knowledge and data driven information from the EcoInvent database. Value functions are usually shaped with the preferences of the decision-makers and/or the relevant experts for each indicator. However, in cases where the experts are not available, a possible solution to shape the value functions is to use existing literature. This approach has been proposed and used in previous studies in the area of water management (Langhans and Lienert, 2016; Langhans et al., 2013). In those papers, the available literature information on several indicators has been used to define the shape of the value functions. We thus tailored that rationale to our specific research, capitalizing upon the available literature from existing database (EcoInvent). We also acknowledge that this type of strategy to make values comparable on a common scale is related to data-driven normalization, as described in literature on CI development (Nardo et al., 2008). In those cases, existing datasets can be used to set the boundaries of best and worst performances, with intermediate performances between them. We have thus conceptualized an approach to shape our value functions by including experts' knowledge (i.e., the research team), as well as elements of data-driven normalization.

For the HeD and ED dimensions, the LCA methodology is applied in order to score all the impact categories related to these two dimensions. To apply this methodology, a cradle-to-gate approach should be considered as system boundaries (Fig. 2), while as the functional unit (FU) “1 kg of product(s) produced”. The reasons for selecting this *technical* functional unit (FU) are: (1) it is a common FU used in the literature for LCA studies and (2) because it is needed to select one in order to create the graphs coming from the 300 chemicals of the Ecoinvent database. This functional unit allows to be adaptable if the user have an input-based FU. For example, if 1 ton of input materials is considered, then, when accounting for the production capacity, all the characterization factors could be transformed to a product-based FU as the one considered in our research. The same happens to the case studies in which various products are produced, applying mass, economic or energy allocation to all the products obtained, the final FU could be considered as 1 kg of products in total. The flexibility and extensive use that provides this FU has been the main reasoning of selecting it as the basis of the methodology, which could be applicable and further specified, and also in cases studies in which variable amounts of materials are needed to perform the same function. Regarding the system boundaries, the reason of considering a cradle-to-gate is because the CI proposed is focused on the technology and product development level, rather than on the end-of-life phase. But, at the same time, it should be noted that, with the circularity indicators the end-of-life stage is partially considered, as product recyclability and waste to landfill are part of the assessment. Lastly, product environmental footprint methodology (PEF) should be used, as it is the one recommended by the EC-SSbD framework (Abbate et al., 2024).

As the emerging processes and technologies are at a low technology

Table 5
Scoring of minimum, percentiles and maximum values from the 300 chemicals impact scores using EcoInvent database.

	Score
Minimum	1.00
Percentile 10	0.90
Percentile 20	0.80
Percentile 30	0.70
Percentile 40	0.60
Percentile 50	0.50
Percentile 60	0.40
Percentile 70	0.30
Percentile 80	0.20
Percentile 90	0.10
Maximum	0.01

Table 6
Example of how the graphs and logarithmic equations were created using the impact category of "human toxicity–cancer".

	Impact value	Score
Minimum	$3.88 \cdot 10^{-12}$	1.00
Percentile 10	$9.19 \cdot 10^{-11}$	0.90
Percentile 20	$2.20 \cdot 10^{-10}$	0.80
Percentile 30	$3.02 \cdot 10^{-10}$	0.70
Percentile 40	$4.98 \cdot 10^{-10}$	0.60
Percentile 50	$8.49 \cdot 10^{-10}$	0.50
Percentile 60	$1.59 \cdot 10^{-10}$	0.40
Percentile 70	$2.58 \cdot 10^{-9}$	0.30
Percentile 80	$5.67 \cdot 10^{-9}$	0.20
Percentile 90	$1.63 \cdot 10^{-8}$	0.10
Maximum	$2.46 \cdot 10^{-6}$	0.01

readiness level (TRL), it is not accurate and fair to compare them with production processes and technologies at high TRL, which are well established and optimized. This would create an unrealistic disadvantage for the penetration and enhancement of new production and technological models. Consequently, to provide a comparative framework, we accounted for the fact that when scaling-up from laboratory level (low TRL) to commercial scale (high TRL) a reduction of impact and damage potentials of even more than 90 % (de Souza et al., 2023) or by a factor of 6.5 (Piccinno et al., 2018) can be achieved. Bearing this in mind, in order to make low TRL and high TRL production processes and technologies comparable, the characterization values obtained per impact category under analysis are multiplied by 0.10. It should be mentioned that, as it is a quite optimistic improvement, sensitivity assessments have been proposed for this value, considering also 0.15 and 0.20 as the multiplying factor.

With respect to the "hazard dimension", a qualitative score was shaped following the three categories reported in Table 1, namely 'most harmful substances', 'substances of concern', and 'other hazards' properties. If any of the materials required for the processing are categorized as "most harmful substances", it is not possible to continue with the assessment. If they are categorized as "substance of concern", the score is 0.5 and if categorized as "other hazards" properties, the score is 1 (the impact of these scores is checked in the sensitivity analysis in Section 2.2.3). To this end, this dimension has a "cut-off" rule, raising awareness and concern among innovators and product developers, in line with the early warning strategy applied in the EC-SSbD framework guidelines (Caldeira et al., 2022a, 2022b).

For the "health" and "environmental" dimensions the value functions were developed from the impact scores of 300 chemicals from the EcoInvent database (Wernet et al., 2016), considering PEF as the methodology for scoring the impact categories. This EcoInvent database is one of the most recognized LCA databases with more than 20,000 reliable datasets on life cycle inventory data related to chemicals, energy, natural resources, waste management, and transport services, among others. It is considered a transparent, reliable, and consistent database, regularly updated and used by more than 5000 organizations.

The impact category scores for the 300 chemicals were analyzed as follows: the minimum impact value was assigned the best score of 1 as the most desirable (most sustainable alternative), while the maximum impact value was assigned the worst score of 0.01 as the least promising.

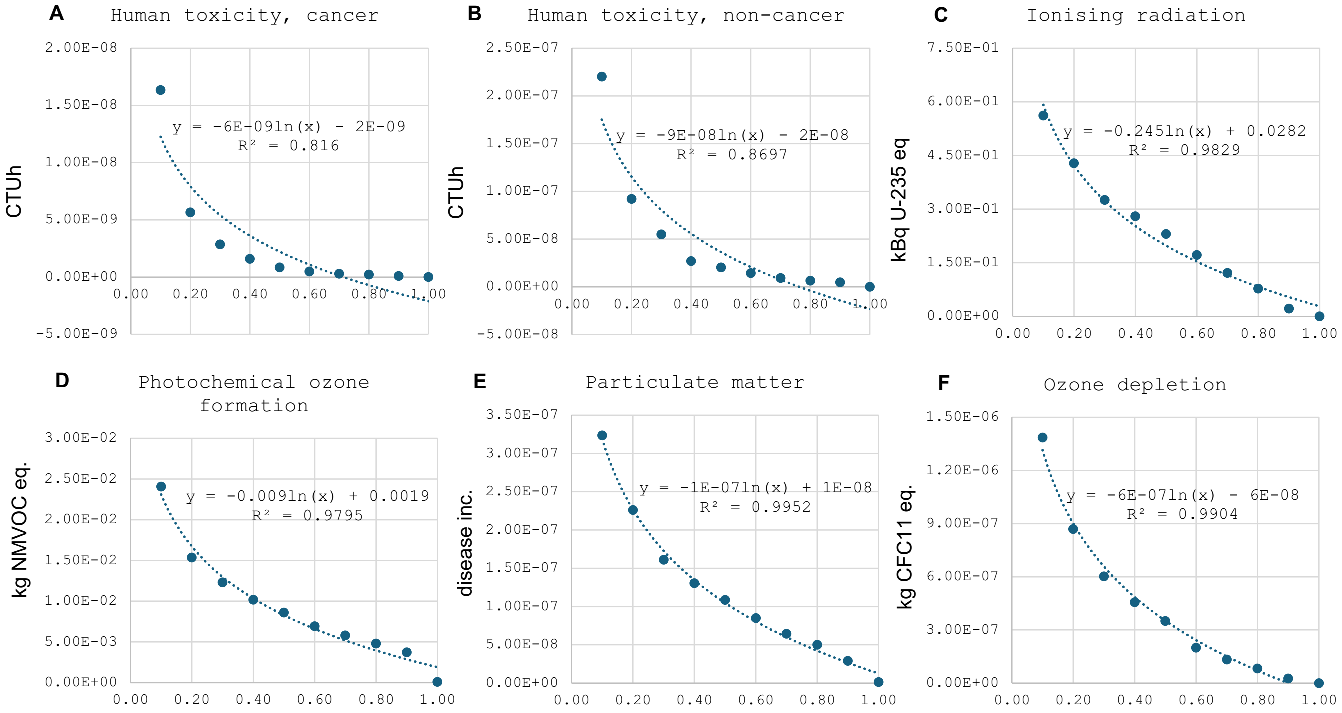

Fig. 3. Graphical and equation models for scoring the "health and risk" dimension. The x-axis represents the individual score per impact category under assessment, while y-axis represents the values obtained for the minimum and percentiles impact scores according to 300-compounds of the EcoInvent database.

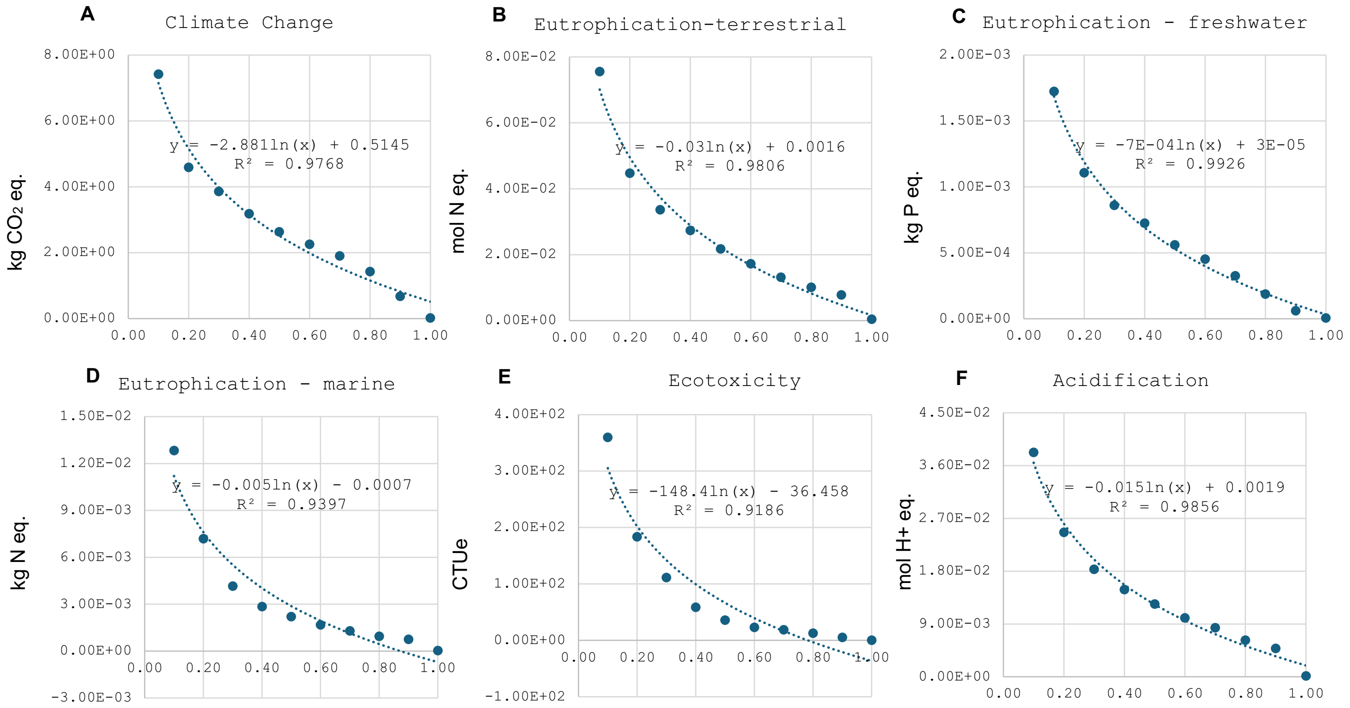

Fig. 4. Graphical and equation models for scoring the "environmental" dimension. The x-axis represents the individual score per impact category under assessment, while y-axis represents the values obtained for the minimum and percentiles impact scores according to 300-compounds of the EcoInvent database.

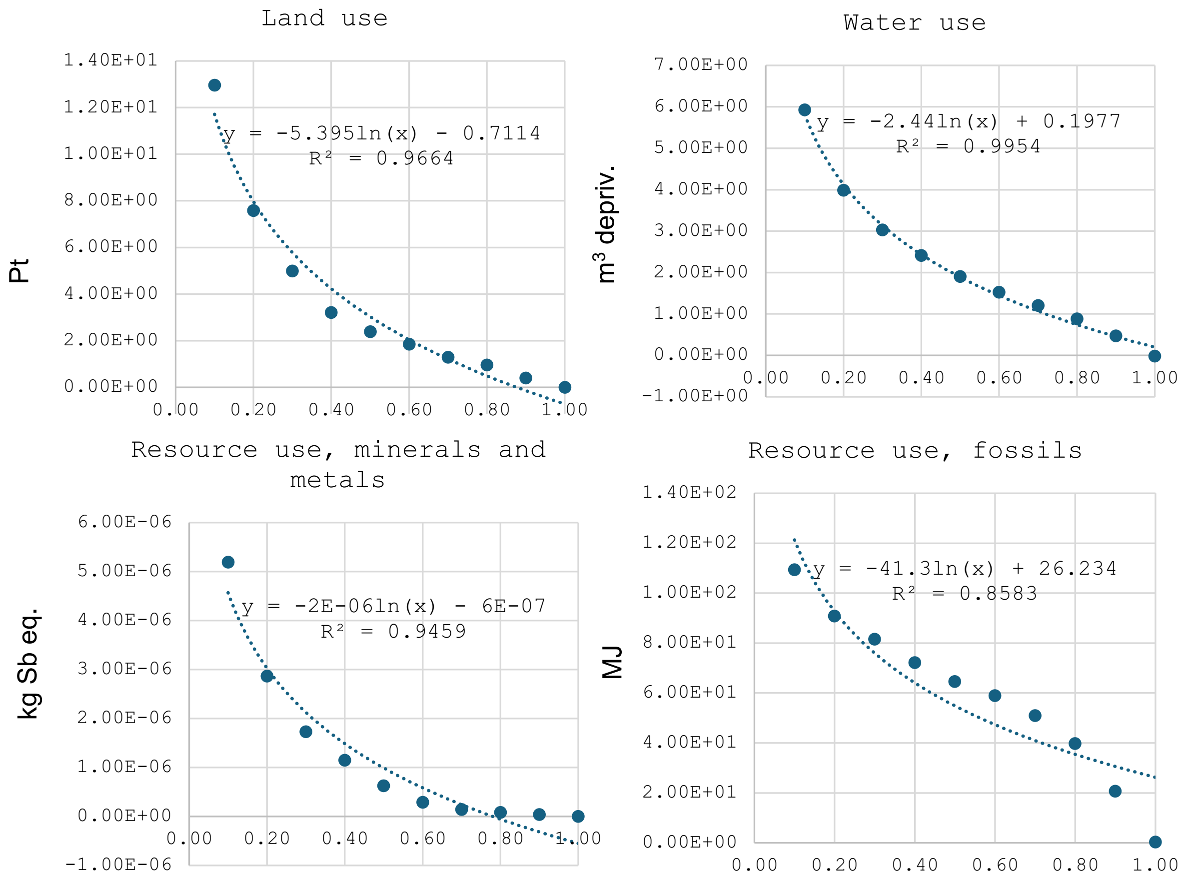

Fig. 5. Graphical and equation models for scoring the "environmental" dimension. The x-axis represents the individual score per impact category under assessment, while y-axis represents the values obtained for the minimum and percentiles impact scores according to 300-compounds of the EcoInvent database.

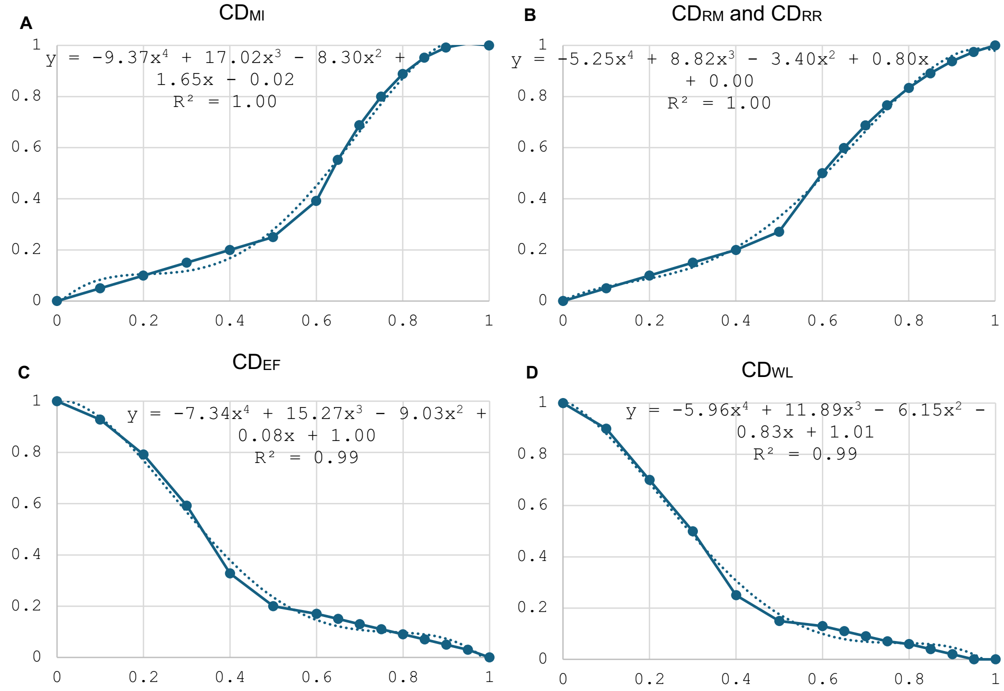

Fig. 6. Graphical and equation models for scoring the "circularity" dimension. The x-axis represents the individual score per impact category under assessment, while y-axis represents the possible values for the circularity indicators. A: CD_{MI}, B: CD_{RM} and CDRR, C: CD_{EF} and D: CD_{WL}. Acronyms: CD_{MI} (Circularity Indicator – Material Intensity Index), CD_{CRM} (Circularity Indicator – Critical Raw Materials), CD_{RM} (Circularity Indicator – Renewable Materials), CD_{EF} (Circularity Indicator – E-factor), CD_{WL} (Circularity Indicator – Waste to Landfill), CD_{REC} (Circularity Indicator – Recyclability), CD_{RR} (Circularity Indicator – Recirculation Rate).

The impact values between these extremes were defined based on the calculation of percentiles, from the 10th to the 90th percentile. This score is reported in Table 5.

Subsequently, in order to provide graphical representation and logarithmic equation models for each of the impact categories under the “health and risk” and “environmental” dimensions, the impact value (minimum, percentiles and maximum) per impact category is represented on the “y-axis” and the score applied (from 0.01 to 1) on the “x-axis”. As an example, the values for the human toxicity cancer category are shown in Table 6, together with the graphical model and the logarithm-based equation, depicted in Fig. 3A.

The same approach was considered for the rest of the impact categories, both for the HeD and ED dimensions. The graphical models, together with the equations for scoring are reported in Fig. 3, in the case of the HeD dimension, and in Figs. 4 and 5 for the environmental one. The dots on the figures represent the all the scores, as exemplified on Table 6.

In the case of the circularity dimension, two qualitative and five quantitative indicators are included. The first qualitative indicator is the one that analyses the presence of critical raw materials and the second one addresses whether the product(s) obtained are recyclable. A binary value function is applied for both indicators, where the lowest score (0.01) is applied if critical raw materials are present or if the resulting products are not recyclable. Otherwise, a score of 1 is used.

The justification for the presence of critical raw materials (CRM) is that there is a high concern about their use, mainly because they are widely required for the construction of renewable energy equipment, such as solar panels or wind turbines, among others (Radebe and Chipangamate, 2024; Chipangamate and Nwaila, 2023). Given this, if the use of CRMs is not controlled, it could lead to their future scarcity, similar to what happened with fossil resources, and this must be avoided. In fact, the European Commission has created a list of CRMs (European Commission et al., 2023), as well as a regulation of the Critical Raw Materials Act (European Commission, 2024), willing to establish a framework to ensure the long-term supply of CRMs.

The same reasoning was considered for the recyclability indicator. If the product or products derived from the process are recyclable, the value of the indicator is 1, while if this is not the case, a value of 0.01 (minimum possible value) is assigned. The recyclability potential is considered a key aspect of the transition towards a circular bioeconomy, as it could promote valorisation strategies, reduce environmental damage and thus enhance more suitable end-of-life scenarios (Ali et al., 2022; Stegmann et al., 2020; Leipold and Petit-Boix, 2018).

In the case of the quantitative indicators, for the CD_{MI} indicator, the value of the score follows the equation provided in Fig. 6A, while in the case of CD_{RM} and CD_{RR} indicators, the equation provided in Fig. 6B is used for scoring. The figures and equations related to CD_{EF} and CD_{WL} indicators are depicted in Fig. 6C and D.

Finally, in the case of the “economic dimension”, the Net Present Value (NPV), the payback period (PP) and the minimum selling price (MSP) were taken into account. In terms of the NPV, if it is negative, it means that the process under evaluation is not economically viable, then the resulting score is 0.01; if it is positive, the value is 1. In the case of the payback period, it should be compared with the useful life of the project. If the PP is longer than the useful life of the project, the score is 0.01, as this means that the initial investment will not be recovered within the useful life of the project. In this case, the revenues are not sufficient to recover the invested capital and to sustain the operating costs of the process, so it is not economically viable. Conversely, if the PP is less than the project lifetime, the score is 1.

With respect to the MSP, it should be compared to the average market price for the same or a similar product. Since new emerging products are often less optimized than those available on the market, it could be difficult to achieve the same or even a lower selling price. For this reason, in this case, a graphical and equation model was made. The score of the x is a ratio between the MSP achieved for the product and the average market value of the product. If the minimum selling price of the evaluated product is equal to the average selling price of the same or a similar product already on the market, then the score is 0.5 (this assumption is checked in the sensitivity analysis in Section 2.2.3). In all

Table 7
Quantitative and qualitative scoring color code. Acronym: Composite Indicator – Safe and Sustainable by Design and Circularity (CI-SSbDC).

CI-SSbDC score	**1**	**0.80**	**0.60**	**0.40**	**0.20**	**0.01**
Color code	🟩	🟩	🟨	🟧	🟧	🟥
Degree of improvement required	Very low	Low	Medium	High	Very high	Need to redesign
Qualification	Safe and Sustainable	High score	Promising score	Medium score	Low score	Not adequate

other cases, Eq. (1) is used:

$$EcD_{MSP}score = -0.55x + 1 \tag{1}$$

where EcD$_{MSP}$ score represents the value between 0.01 and 1 achieved for the “minimum selling price” indicator in the economic dimension and x is a ratio between the MSP achieved for the product and the average market value of the product. It should be mentioned that, if achieved a value lower than 0 (negative), then a value of 0 is considered for the EcD$_{MSP}$ score, while if the score achieved for Eq. (1) is higher than 1, then the value of the score is considered as 1. The range of the EcD$_{MSP}$ score should be always between 0.01 and 1. Besides, as x is a ratio between the MSP obtained and the average of the market, it has not units, x is adimensional.

2.2.2. *Aggregation algorithms for the Composite Indicator – Safe and Sustainable by Design and Circularity (CI-SSbDC) dimensions*

The CI-SSbDC can be calculated using Eqs. (2)–(4), where all the dimensions are combined to provide the final score for each alternative, considering the three aggregation methods. Given this, three different scores of the CI-SSbDC are obtained, one for the additive aggregation (Eq. (2)), one for the geometric (Eq. (3)), and the last one for the harmonic aggregation model (Eq. (4)).

$$CI - SSbDC_{add} = w{\cdot}HD + w{\cdot}HeD + w{\cdot}ED + w{\cdot}CD + w{\cdot}EcD \tag{2}$$

$$CI - SSbDC_{geo} = HD^{w}{\cdot}HeD^{w}{\cdot}ED^{w}{\cdot}CD^{w}{\cdot}EcD^{w} \tag{3}$$

$$CI - SSbDC_{har} = {}^{1}\Big/\left(\frac{w}{HD} + \frac{w}{HeD} + \frac{w}{ED} + \frac{w}{CD} + \frac{w}{EcD}\right) \tag{4}$$

where w represents the weighting factor (assumed to be equal for each dimension and indicator), HD is the factor for the hazard dimension, HeD the one for health and risk dimension, ED represents the environmental dimension, CD the circular dimension and EcD represents the economic dimension.

It is important to reflect on the crucial step of weighting in MAVT, where the weighting factors represent the trade-offs between the indicators. As for all MCDA methods that use weights, it is necessary that the relevant weighting methods are chosen to elicit them. For MAVT, for example, the trade-off and SWING methods are the ones that are suitable (Bottero et al., 2014; Keeney, 2020).

The combination of weights and indicators results in the overall score between 0.01 and 1. To aid its understanding, a rating in preference-ordered categories is commonly used when shaping CIs. This is the case in SSbD-related work (Caldeira et al., 2022a, 2022b), environmental management research, and sustainability of chemical processes (Saling et al., 2024; Pinto et al., 2020; Reichert et al., 2015).

The CI-SSbDC composite indicator can have a value between 0 and 1, with 1 being the best value with a very low degree of improvement required and represented with a color of “dark green”. The worst case is a score of 0, which implies that the overall performance of the alternative is very low, and thus requires redesign, and is represented with the “red” color. The intermediate values of our CI are shown in Table 7.

Table 8
Overview of the sensitivity analysis with the different model versions of CI-SSbDC tested in this research. Acronym: technological readiness level (TRL), minimum selling price (MSP), health dimension (HeD), economic dimension (EcD), hazard dimension (HD).

Model version (V)	Value functions		Dimension affected	Aggregation function
	TRL factor	Alternative		
V1	0.10	Initial version	All	Additive
V2			All	Geometric
V3			All	Harmonic
V4	0.10	−0.2 for “substances of concern” indicator originally considered as 0.5	HD	Additive
V5			HD	Geometric
V6			HD	Harmonic
V7	0.10	+0.2 for “substances of concern” indicator originally considered as 0.5	HD	Additive
V8			HD	Geometric
V9			HD	Harmonic
V10	0.10	−0.2 for “MSP” indicator originally considered as 0.5	EcD	Additive
V11			EcD	Geometric
V12			EcD	Harmonic
V13	0.10	+0.2 for “MSP” indicator originally considered as 0.5	EcD	Additive
V14			EcD	Geometric
V15			EcD	Harmonic
V16	0.10	Change the worst value from 0.01 to 0.10	All	Additive
V17			All	Geometric
V18			All	Harmonic
V19	0.15	Initial version	HeD and ED	Additive
V20			HeD and ED	Geometric
V21			HeD and ED	Harmonic
V22	0.20	Initial version	HeD and ED	Additive
V23			HeD and ED	Geometric
V24			HeD and ED	Harmonic

Due to the lack of existing thresholds to separate them, equal intervals were used, following a common solution in environmental decision-making (Reichert et al., 2015). The aggregation formulas used to calculate the individual scores of each dimension are described in the Supplementary material.

2.2.3. *Sensitivity analysis*

The development of CI includes methodological choices that influence the final score. Sensitivity analysis is a good solution to assess model stability, and it is recommended to understand whether and to what extent the input data and model structure affect the final model outcome (Opon and Henry, 2020; Nardo et al., 2008). Since a key methodological novelty of CI-SSbDC lies in the use of value functions, the sensitivity analysis has focused on these components of the model. In this work, only indicators that were directly assessed by the research team (therefore, the most subjective) were included in the sensitivity analysis, and not those whose value functions were created using the databases (EcoInvent), which could be tested as future research. Based on this rationale, the indicators that were included in the sensitivity analysis were only the ones with intermediate scores between the best

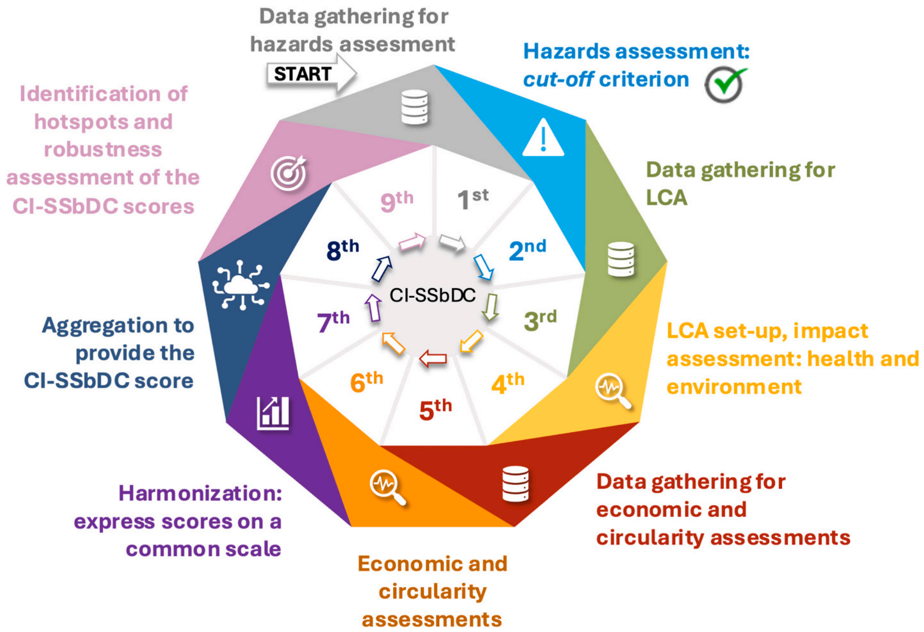

Fig. 7. Methodological steps for calculating the CI-SSbDC (Composite Indicator – Safe and Sustainable by Design and Circularity).

and the worst performances chosen by research team:

- hazard dimension, hazard information: 0.5 for "substance of concern".
- economic dimension, minimum selling price (MSP): 0.5 for MSP of the product under assessment equal to the average selling price of the same or similar product already in the market.

Because there are no guidelines defining how much the value functions should change in the sensitivity analysis, it has been applied a ± 0.2 increase and decrease to the intermediate values of the functions.

In addition to testing the sensitivity of the scoring of the indicators mentioned above, we also studied the effect of changing the worst value of each value function from a value of 0.01 to a value of 0.10. This choice was based on previous research on sensitivity studies (Cinelli et al., 2021) and allows assessing the stability (or not) of the model in terms of how low the worst performance on each criterion for each value function may be. Besides, as previously mentioned, also sensitivity assessments were proposed for the multiplying factor considered for the TRL, as base case 0.10, concretely changing it for 0.15 and 0.20.

These different set-ups of the sensitivity analysis led to 24 model versions of the CI-SSbDC by combining the different value functions with the aggregation functions. These are summarized in Table 8, also showing the dimensions affected for each version of the model.

2.3. Illustrative application of the framework

2.3.1. Methodological description

In order to apply the MCDA model proposed, nine steps are required, which are depicted in Fig. 7, and explained below.

1st Data gathering for hazard assessment. Identification of all chemical-based inputs to the process.

2nd Hazards assessment: cut-off criterion. For all the identified chemicals from the 1st step, analyze the hazards (health, environment and physical) according to the methodology of HD dimension. Data sets and/or safety data sheets should be used to compile the hazards associated with the chemical inputs. If any of the chemicals are classified as the "most harmful substances", the assessment cannot be continued.

3rd Data gathering for LCA. If the first analysis passes the cut-off criterion, all mass and energy balances should be developed in order to collect all the data necessary to develop the life cycle inventory.

4th LCA set-up, impact assessment: health and environment. For this stage, 1 kg of produced product should be considered as the functional unit, and also a "cradle-to-gate" approach as system boundaries. In terms of methodology, PEF should be selected. Within this step all the indicators required for the scoring of HeD and ED are obtained, that needs to be further analyzed on following steps of the methodology.

5th Data gathering for economic and circularity assessments. All the data regarding cash flow analysis, market average product selling price, waste management strategies and process flows should be gathered.

6th Economic and circularity assessments. Scoring of the indicators identified for the EcD and CD.

7th Harmonization. All the scores obtained for the indicators that conform the HD, HeD, ED, EcD and CD are expressed on a common scale, using the proposed value functions with their respective equations.

8th Aggregation to provide the CI-SSbDC score. Once all the scores are harmonized, aggregation is applied, in order to get a single score between 0.01 and 1. Three aggregation models are used: additive, geometric and harmonic. Final score of the CI-SSbDC and qualitative and quantitative classification according to the guidelines of Table 7.

9th Identification of hotspots and robustness assessment of the CI-SSbDC scores. As the shapes of the value functions have been based on research team's decision, in order to evaluate the robustness of the CI-SSbDC proposed, various sensitivity analysis have been proposed to assess the effect of such choices on the final score and categorization of the CI-SSbDC.

2.3.2. Definition of case studies

Three case studies are used for CI-SSbDC validation, using several bio-based waste streams to produce a functional and bioactive product: nisin. Nisin is an antimicrobial and bioactive compound categorized as a GRAS (Generally Recognized As Safe) compound by the U.S. Food and Drug Administration and the World Health Organization (WHO) (Tavares et al., 2023). For the CI-SSbDC application, three case studies were considered according to the type of waste material used to obtain

Table 9
Brief description of the case studies (CS).

Case study (CS)	Product	Bio-waste input	Process description		Reference
CS 1	Nisin	Sugar beet pulp	Pretreatment: heat treatment combined with centrifugation, followed by enzymatic hydrolysis	Fermentation process using *Lactococcus lactis* as strain for 24 h. Downstream process consisting on acidification, precipitation, centrifugation and spray drying.	(Arias et al., 2021a, 2021b)
CS 2		Corn stover	Pretreatment: autohydrolysis and enzymatic saccharification		
CS 3		Cheese whey	Pretreatment: heat treatment combined with centrifugation		

the product of interest: nisin. The input biowastes are sugar beet pulp, corn stover and cheese whey (Arias et al., 2021a, 2021b). A brief summary of the case studies is included in Table 9, bearing in mind that these case studies have been previously developed and published by the authors.

3. Results

3.1. *Composite Indicator – Safe and Sustainable by Design and Circularity (CI-SSbDC) applied to three case studies*

All the metrics and methods proposed in the previous sections have been applied to each of the alternative CS. The scores obtained per each case study and considering the three aggregation models are depicted on Table 10.

As could be observed, the same HD value is obtained for all cases. The reason behind this is that there is only one chemical (methanol) classified as “Substance of concern”, used in the downstream section of the process for the purification of the lactic acid, but, even though, all CSs exceed the cut-off criterion (HD). Regarding the other dimensions, in the case of HeD, the most outstanding is CS1, with values between 0.38 and 0.49, while the others have significantly lower scores. It is worth mentioning that, in this HeD dimension, there is more similarity between the scores obtained for each of the indicators that make up its calculation, achieving a maximum variation in the case of CS1 (± 0.06), while only ±0.02 for CS2 and CS3. This fact could be observed when switching from an additive aggregation method to a geometric and harmonic one, since in all cases the variance of the score obtained is below 0.15.

In contrast, when evaluating the ED dimension, especially for CS2 and CS3, the differences between the application of the additive and harmonic method amount to 0.62 and 0.69, respectively, which implies going from a “Medium CI-SSbDC score” to a “Not-adequate CI-SSbDC score” in this individual dimension. This observation is a clear example of how the aggregation method could effect on the economic potential and viability of a process or technology alternative.

In the case of CD, a similar effect is observed; the fact that a very low value (close to 0) is obtained for one of the indicators considered for the assessment of this dimension does not imply a significant effect on the additive aggregation method, but it does for the geometric one, and even more so for the harmonic one. It is therefore better to have a process scheme, technology or other scenario that remains more or less stable in the scores obtained for the indicators and metrics rather than performing very well in some of them, while performing very poorly in others, as this will be penalized when considering geometric and harmonic aggregation methods. Finally, for EcD, the most efficient alternatives from the point of view of financial viability are most clearly seen, and there is not much difference between the application of one aggregation method or another.

For the final CI-SSbDC score and categorization it could be observed that, at least, moving from one aggregation method to another implies the loss of one level in the score. This is clearly observed in the CS1, represented on Fig. 8, in which for additive aggregation method the final CI-SSbDC score achieved 0.72, thus being a “Promising score”, while for geometric method the value is reduced to 0.60, categorized as “Medium score” and for harmonic method the score is significantly reduced to 0.21, thus being a “Low CI-SSbDC score”. Besides, it was possible to clearly see hot spots per dimension for the scenario under study, useful to identify the aspects to be improved in order to obtain a higher final score of the CI-SSbDC indicator (Fig. 8).

On the other hand, when assessing various case studies, it is also fundamental to have a comparison graph, in order to evaluate the one

Table 10
Overall scores of the CI-SSbDC, as well as for each dimension. Acronyms: Agg. (aggregation), A (additive), G (geometric), H (harmonic), CS1: Case Study 1, CS2: Case Study 2, CS3: Case Study 3, CI-SSbDC: Composite Indicator – Safe and Sustainable by Design and Circularity. Categorization and color code according to Table 7.

Case study	Agg.	HD	HeD	ED	CD	EcD	CI-SSbDC	Categorization
CS1	A	0.94	0.44	0.88	0.48	0.83	0.72	Promising CI-SSbDC score
	G	0.94	0.42	0.84	0.29	0.79	0.60	Medium CI-SSbDC score
	H	0.94	0.38	0.77	0.06	0.75	0.21	Low CI-SSbDC score
CS2	A	0.94	0.04	0.67	0.42	0.17	0.45	Low CI-SSbDC score
	G	0.94	0.02	0.30	0.22	0.04	0.14	Not adequate CI-SSbDC score
	H	0.94	0.02	0.05	0.05	0.01	0.03	Not adequate CI-SSbDC score
CS3	A	0.94	0.04	0.78	0.44	0.83	0.61	Medium CI-SSbDC score
	G	0.94	0.02	0.50	0.20	0.79	0.28	Low CI-SSbDC score
	H	0.94	0.02	0.09	0.03	0.75	0.05	Not adequate CI-SSbDC score

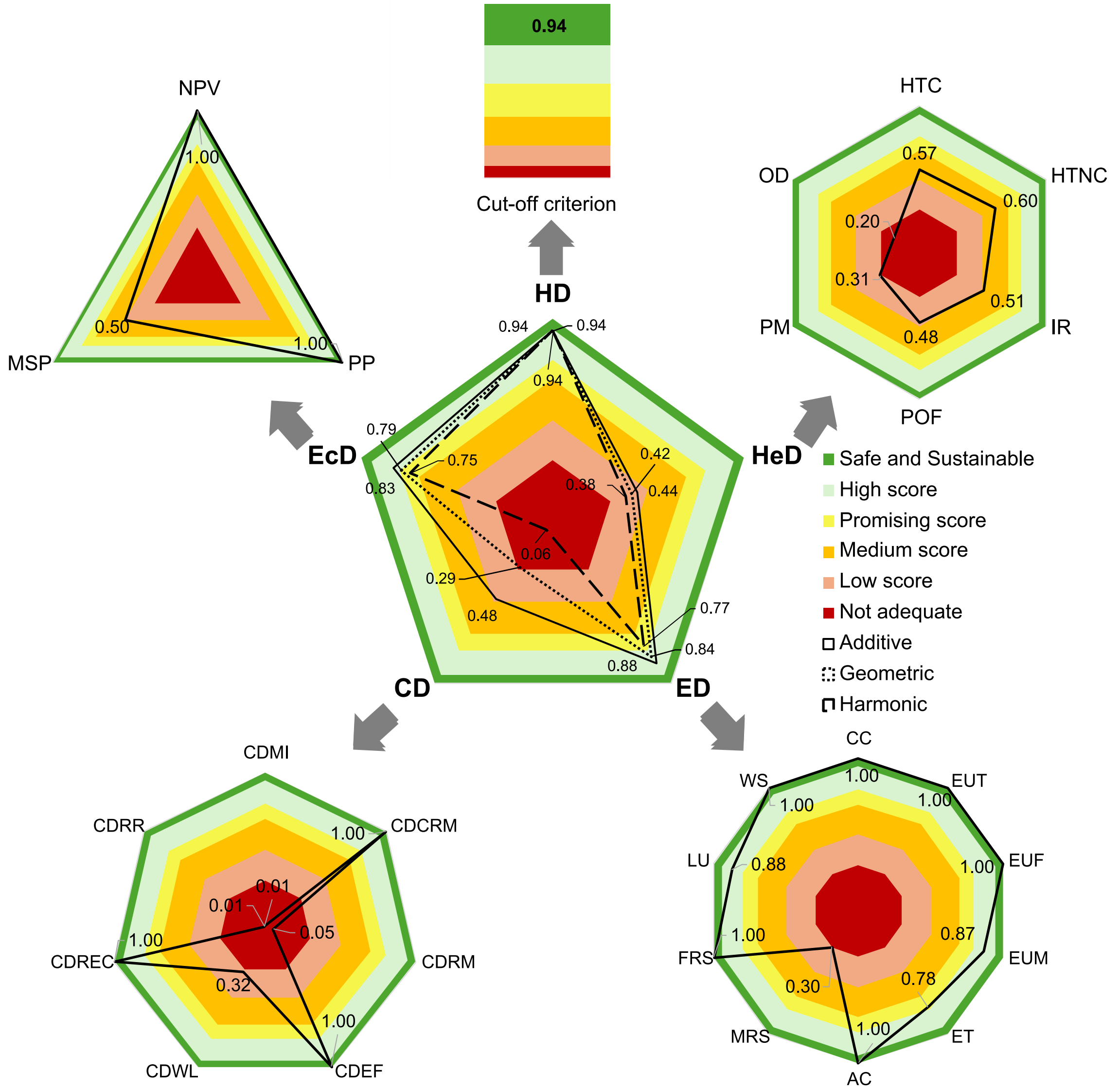

Fig. 8. Graphical representation of CI-SSbDC final score per dimension and individual scores achieved for CS1: Nisin from sugar beet pulp. Color code according to Table 6. In the central figure: the additive model is represented by continuous line, the geometric one by dotted line and the harmonic one by discontinuous line. Acronyms: HTC (human toxicity carcinogenic), HTNC (human toxicity non carcinogenic), POF (photochemical ozone formation), OD (ozone depletion), PM (particular matter), IR (ionizing radiation), CC (climate change), ET (ecotoxicity), AC (acidification), RM (resources, mineral), WU (water use), RF (resources fossil), LU (land use), EUM (eutrophication marine), EUT (eutrophication terrestrial), CD_{REC} (recyclability), CD_{RR} (recirculation rate), CD_{RM} (renewable materials), CD_{WL} (waste to landfill), CD_{EF} (E-factor), CD_{MI} (material index), CD_{CRM} (critical raw materials). NPV (net present value), MSP (minimum selling price), PP (payback), EcD: economic dimension, HD: hazard dimension, HeD: health dimension, CD: circularity dimension, ED: environmental dimension.

that provides the best performance under the EC-SSbD and circularity perspectives. Fig. 9 is useful to compare the values obtained when several case studies are being evaluated for obtaining the same product with different raw materials, or it could also be the case of obtaining different products with a single raw material, or even evaluating several process technologies to obtain the same product. To this end, Fig. 9 shows whether the case studies under evaluation pass the cut-off criterion and which production model is the most suitable from the point of view of each of the pillars of sustainability and circularity. Each quadrant of the figure represents a dimension, with each of the axis extremes representing the most sustainable and circular (i.e. the highest value of the CI-SSbDC dimension), while the center (0.0) represents the worst possible result, where the production model under assessment needs to be redesigned.

3.2. Sensitivity analysis of the Composite Indicator-Safe and Sustainable by Design and Circularity (CI-SSbDC)

The comparison of multiple case studies is performed via the sensitivity analysis as described in Section 2.2.3. This strategy allows studying how stable the final scores of the CI-SSbDC are according to different versions of the value functions. These scores are presented in Table 11 (the codes used in this Table 11 are explained on Table 8). As it could be observed, changing the indicator of the **substance of concern** (**V4-V9**) does not imply a significant variance on the final score given the fact that, for the case studies under assessment, there are not substances of concern that could imply a low value in this dimension.

In the case of the **MSP** sensitivity assessment (**V10-V15**), even the score does not change significantly by varying the parameter from 0.5 to 0.3 and 0.7. In some cases, a variation on the final classification of the scenario is observed. This is the case of CS1 – geometric aggregation model - from medium to promising when using +0.2 MSP (**V14**), CS3 –

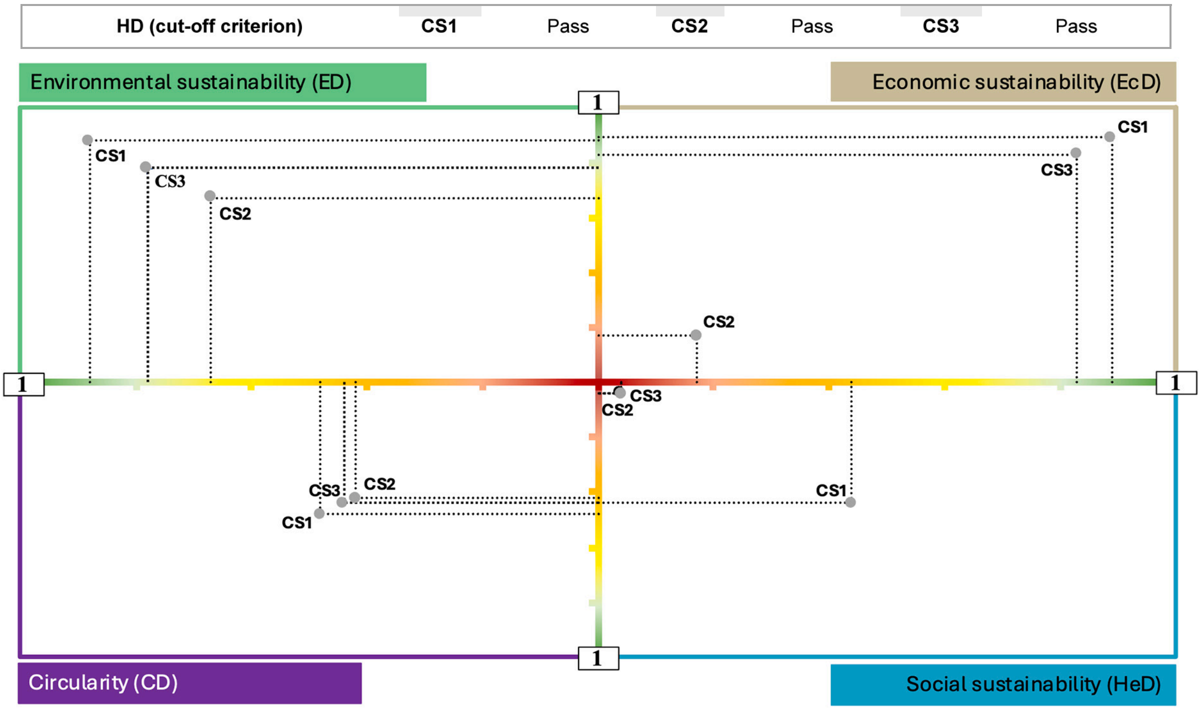

Fig. 9. Graphical comparison of the dimensions scores of CI-SSbDC of all scenarios considering additive aggregation model. Acronyms: CS1: Nisin from sugar beet pulp, CS2: nisin from corn stover, CS3: nisin from cheese whey. Color code x-y axis according to Table 7.

additive aggregation model – from promising to medium when using −0.2 MSP (**V10**). For the other scenarios, even when the final scores are slightly modified, it does not imply a change on the categorization and qualification according to Table 6.

On the contrary of what happened with the previous sensitivity scenarios, when assessing the change on the minimum possible score from 0.01 (base case) to 0.1 (**V16-V18**), significant changes are observed for the geometric and harmonic aggregation models. In fact, CS2 and CS3 showed 1-level variation when geometric aggregation model is applied, in the case of CS2 from “not adequate-need to redesign” to “low score”, while for CS3 from “low score” to “medium score”. For the harmonic aggregation model, only CS3 shows variation, concretely from “not adequate – need to redesign” to “low score”. On the contrary, CS1 maintains its classification for all aggregation models considered.

In the case of the TRL factor sensitivity assessments (**V19-V24**), no significant differences are found in the final classification of the case studies compared to previous sensitivity assessments. The only changes that are observable, implying a variation on the final classification obtained, were in the harmonic aggregation model, which results in a change from “low score” to “not adequate-need to redesign” for CS1.

To this end, given the scores obtained, it could be stated that the parameter that implies greater variation in the final value of the CI-SSbDC composite indicator is the minimum score value (i.e. 0.01 to 0.1).

In order to aid the interpretation of the multiple versions of the CI-SSbDC, boxplots are proposed in Fig. 10. Box plots are useful solutions for grouping scores on the CI-SSbDC in an easily understandable format. The box represents 50 % of the data points that range between the 25th and 75th percentiles in the given data set, while the minimum and maximum values are represented by the whiskers. Besides, also the median (i.e. 2nd quartile), is represented (horizontal straight line inside the box), that marks the mid-point of the data. This representation allows users to identify the variation in the scores obtained, as well as their stability when the score is considered using different aggregation models. For example, with the harmonic aggregation model it is observed that the variability among the scores obtained is small, while the additive and geometric show greater variability in the results obtained, with the geometric aggregation model the one with which widest variability. In the case of CS1 (Fig. 10A), the variability in the scores obtained is significantly increased in the geometric aggregation model (0.16), but the lowest variability on the additive aggregation model is obtained (0.06). CS1 is also the case study with the highest CI-SSbDC scores. CS2 (Fig. 10B) is the one with the lowest scores obtained for both the additive and geometric aggregation models, thus being the one with the highest difference in the final score of the CI-SSbDC when assessing the three aggregation models proposed. The highest variabilities on the aggregation models are observed for CS3 (Fig. 10C), achieving a variance of 0.39 in the case of the additive, 0.31 for the geometric and 0.23 for the harmonic ones.

Overall, CS1 consistently achieves the best performance in terms of the sustainability and circularity perspectives, as it is the one that achieves the highest CI-SSbD score in the majority of the scenarios. On the contrary, CS2 is the one that consistently receives the worst CI-SSbD score, thus resulting in the least promising alternative.

4. Discussion

4.1. Data availability

When developing the methodology, particular attention has been paid to the issue of data availability limitation, and for this reason the authors have focused on shaping a tool that operates with limited data. In the case of the HD dimension, only the safety data on the inputs is required, which could be found on the safety datasheets of the chemicals input materials. For the HeD and ED dimensions, only mass and energy balances for the construction of the LCA inventories are required, which is data usually required when developing a new product and/or technology even at low TRL-scale (de Souza et al., 2023). In the case of the CD dimension, the indicators selected are easy to calculate with mass and energy balances too, one of the preferences for their selection. Lastly, for the EcD dimension, the financial variables under assessment (NPV, payback and minimum selling price of the product) are required

Table 11
Sensitivity assessment results considering the final score of CI-SSbDC for each value case and each case scenario under assessment. Acronyms: CS1: Nisin – SBP, CS2: Nisin – CS, CS3: Nisin – CW, MSP: minimum selling price, TRL: technological readiness level. Color code: following Table 7 guides.

	Base case			−0.2 substance of concern			+0.2 substance of concern		
	V1	V2	V3	V4	V5	V6	V7	V8	V9
CS1	0.72	0.60	0.21	0.71	0.59	0.21	0.72	0.60	0.21
CS2	0.45	0.14	0.03	0.44	0.14	0.03	0.45	0.14	0.03
CS3	0.61	0.28	0.05	0.60	0.28	0.05	0.61	0.14	0.03
	−0.2 MSP			+0.2 MSP			0.10 min. score parameter		
	V10	V11	V12	V13	V14	V15	V16	V17	V18
CS1	0.70	0.58	0.20	0.73	0.61	0.21	0.72	0.45	0.26
CS2	0.44	0.14	0.03	0.46	0.14	0.03	0.48	0.31	0.19
CS3	0.59	0.27	0.05	0.61	0.26	0.31	0.63	0.45	0.26
	0.15 multiplying factor TRL			0.20 multiplying factor TRL					
	V19	V20	V21	V22	V23	V24			
CS1	0.69	0.54	0.19	0.67	0.50	0.17			
CS2	0.44	0.13	0.03	0.44	0.12	0.03			
CS3	0.65	0.27	0.04	0.65	0.27	0.04			

in order to evaluate whether a low-TRL technology or product has the potential to be developed at a larger scale, as these are the parameters required to determine the economic viability and feasibility (Gautam et al., 2024). Given this, the data required for the calculation of the indicators is expected to be available for low-TRL products and technologies too.

4.2. Methodological reasoning

The basis of the value functions created for the HD and ED dimensions of the CI-SSbDC has been the EcoInvent database, considering the impact loads of 300 chemicals available in the database. The reasons for selecting the EcoInvent database are three: (1) the largest amount of data on the chemicals, (2) the most consistent and transparent life cycle database for inventories and (3) the up-to-date information in the database. We anyhow acknowledge that there are other database that could be used for gathering the impact loads and thus creating the value functions, as the case of Agri-footprint (Durlinger et al., 2017) or EU and Danish Input Output (Sustainability, 2020).

Some other aspects to acknowledge are the decisions made over the functional unit and the system boundaries. Similarly to the methodological choices, this selection has been based on usefulness, adaptive and easy-to-handle characteristics. In this respect, this choice allows comparison with other case studies in the literature, as the FU and system boundaries selected are the most common ones being used by LCA practitioners. On the other hand, even though a cradle-to-gate approach has been considered, namely from the extraction of raw materials to the "gate of the factory", it has been somehow extended in the circularity assessment, as end-of-life strategies on the waste produced on the production scheme, as well as the potential recyclability of the produced product, are also being considered in the circularity indicators selected for assessment. In this regard, all the requirements regarding value chain actors and steps required by the SSbD framework have been included in the proposed CI-SSbDC.

Regarding the levels of compensation used when developing the CI, three have been proposed in this article, and they were also applied to the three case studies. According to the chosen aggregation algorithm, significant effects on the final score are achieved, resulting in changes to categorization of some of the scenario under assessment. The research team cannot provide input on the most suitable aggregation algorithm, as that will be dependent on the preference structure of the end-user who is tasked with making a decision.

4.3. Comparison with existing literature

At present, there is not another CI or methodology based on the integration of SSbD and circularity in the literature to compare with the one developed in this research article. The lack of comparison also makes it difficult to identify the gaps and flaws that this proposed CI could have, but it could be considered as a first methodological step to be enhanced and improved in the future, looking to provide a comprehensive, well-developed and strong CI to measure SSbD and circularity performances. Nonetheless, the work developed by Hristozov et al. (2023) employs an MAVT-based methodology to integrate performance, safety and sustainability considerations of chemicals and advanced materials. This confirms the interest and suitability for methodologies based on MAVT to integrate information of different type and preferences of the stakeholders to provide a final decision recommendation.

The developed CI is in line with the multiple articles that have recently proposed roadmaps for SSbD operationalization, by highlighting the current challenges and gaps (Apel et al., 2024; Reins and Wijns, 2024; Sudheshwar et al., 2024). The authors highlight the need of integrating circularity, the essential participation of stakeholders, the necessity of harmonizing the framework and developing standards, as well as trying to anticipate to the regulatory demands by the creation of a future-looking SSbD concept. In view of these requests, the integration of circularity indicators and TRL tailoring in the CI-SSbDC have been done with the purpose of integrating the SSbD framework also for new emerging technologies and products, both bio-based and fossil-based ones. The TRL factor allows to provide a future-forward vision on the potentials and challenges of new technologies in the market value chain, also with the intention to be in line with the coming regulatory frameworks.

Besides, recently, the Government of the Netherlands have developed a collection of essays in which are described the needs and challenges that organizations and stakeholders thinks that are required to be included in the concept of SSbD framework, "Redesigning Chemical Innovation - Essays on Safe and Sustainable by Design" (2024). Analyzing this essay, various common strategies and support statements have been detected. Firstly, the essay state that "the use of substances of concern should not be incompatible with SSbD, rather than in the provision of the best solutions", which supports the choice of hazard value function scores, dependent on the expertise at hand. Secondly, the essay discusses about the need of moving forward the creation of comparative assessment of existing chemicals to provide tools that could also be used for one single product, and this has been the focus of the proposed CI-SSbD, as it could be rather used for a single product or to compare production schemes alternatives. And, thirdly, the essay concerns about the need of developing sustainability and circularity assessments with limited data, for which tools and easy-to-follow methods should be encouraged, as the one proposed in this article.

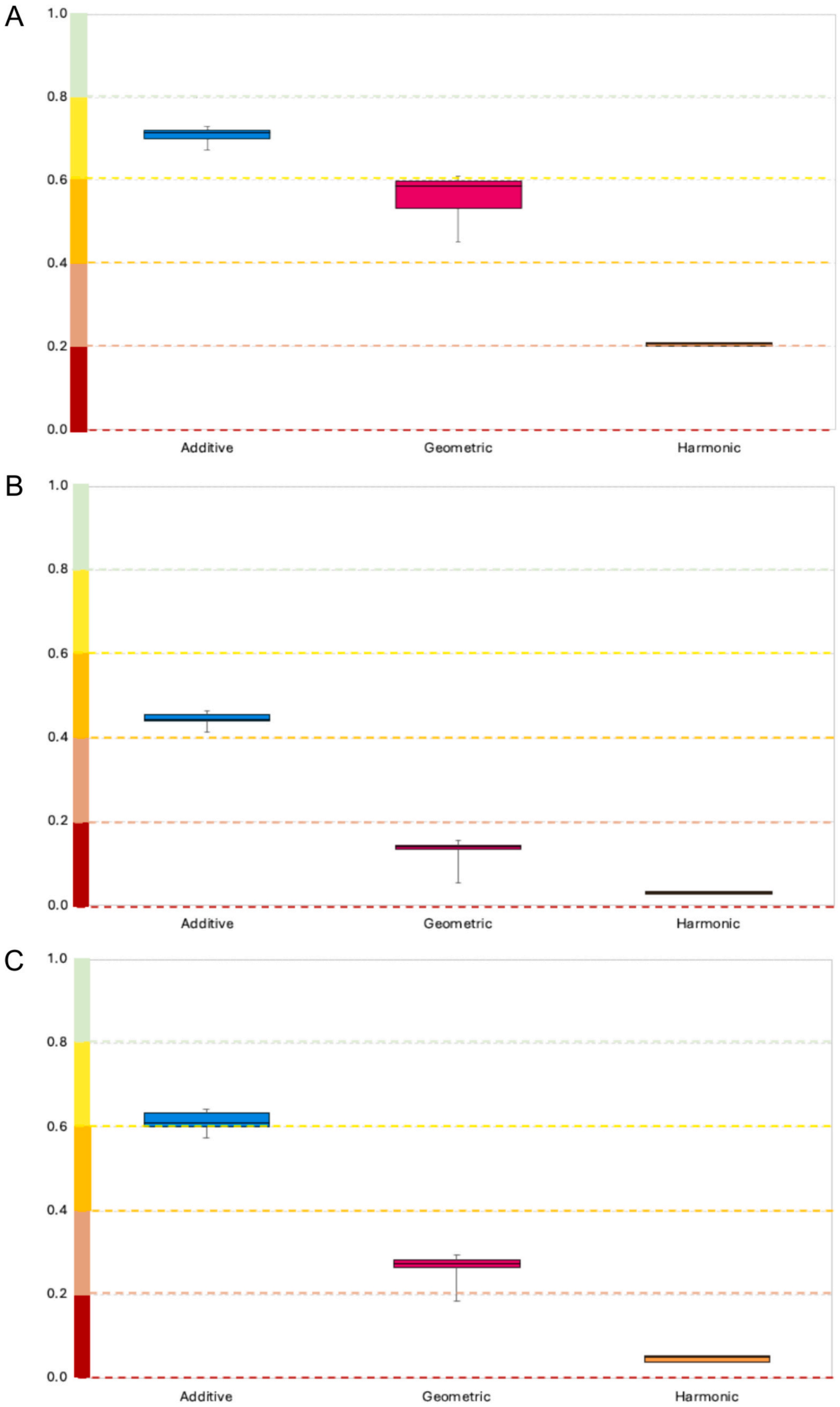

Fig. 10. Summary of sensitivity assessments on the final scores obtained per case study (A: CS1, B: CS2 and C: CS3) according to the aggregation model considered.

4.4. Future research

While the demonstration of the adequacy of the proposed CI based on SSbD and circularity frameworks has been done with already developed and published case studies, it has not been possible to evaluate its adequacy and comprehensiveness also by potential end-users. For this reason, to verify the applicability of the methodology proposed, these end-users' validations (e.g., technology developers, sustainability and circularity experts and practitioners, I&D companies' departments, and academics) should also be performed. Given this, it is recommended, as future research, to test it in more case studies, using different industries as test beds. In addition, it would be valuable to receive feedback from MCDA users and practitioners in terms of the applicability of the methodology, with specific focus aggregation algorithms that fit further preference structures (e.g., interacting indicators). The involvement of experts and stakeholders in the discussion and refinement of the value functions would be a valuable methodological contribution to improve their accuracy and relevancy.

Regarding the impact data, databases other than EcoInvent could be explored, building upon the wide repository presented in the PARC Toolbox (PARC, 2024), for example. Moreover, the development of a toxicological database for new biobased products should be something to consider in the future, as it could provide more information to further and more accurately develop a safety and health assessment, in line with the requirements of the EC-SSbD guidelines and framework.

Besides, it could be also interesting to integrate certification bodies, standards/normalization units, academia and technological developers in order to study whether the indicators selected for the assessment of each of the dimensions of the CI-SSbDC indicator are adequate, sufficient and efficient to assess the sustainability and circularity potential of the case studies under assessment. The integration and collaboration of these bodies could also offer a guide on a forward vision of where to focus to be aligned with new policies, standards and regulations that could arise.

5. Conclusion

In this research article, the principles of the EC-SSbD framework have been combined (i.e. safety, sustainability and circularity), to propose a methodology for quantifying them via five dimensions. We developed a composite indicator, the CI-SSbDC, with the aim of comprehensively scoring products based on their safety, sustainability and circularity performance. The proposed CI is a demonstration of the operationalisation of the SSbD framework. It builds upon some of the most recognized indicators to evaluate the sustainability and circularity potential of a case study related to the chemical sector from an early-stage of design, thus at low TRL. The CI-SSbDC allows practitioners to get a first perspective on which dimension(s) requires immediate attention, as it provides an individual score each of the environmental, economic, social, safety and circularity dimensions. Also, this CI works with scarce data, as only mass and energy balances are required, together with a preliminary version of an economic assessment to evaluate the economic viability.

The contributions of the proposed CI-SSbDC are six-fold. *First*, all the dimensions of sustainability and circularity have been included, as recommended by the European Commission in the SSbD guidance and technical report. *Second*, it has been shown how it is possible to follow a structured selection process for the identification of the suitable decision support method within the SSbD framework requirements. This resulted in the choice of value-focused thinking, which enabled the development of harmonized value functions to score each indicator and dimension in the CI-SSbDC on a common scale. *Third*, the operationalization of different SSbD-related decision-making preferences has been enabled by the selection of three different aggregation algorithms. These allow accounting for decision-makers that accept different levels of compensation between the indicators and dimensions used in the CI-SSbDC. *Fourth*, a procedure to study the stability of the CI-SSbDC has been introduced, by testing how stable the final outcome of the model is according to some key methodological choices made in its development. *Fifth*, the proposed CI-SSbDC can be used for performing assessment of a single case study as well as to compare multiple case studies at the same time. It thus supports comparative and non-comparative assessments. And, *sixth*, sustainability and circularity, which are usually are assessed separately, are accounted for at the same time in our CI-SSbDC.

The applicability of the CI-SSbDC was then showed for one product with three different production feedstocks. It demonstrated the two main uses that can be made of this CI to help process developers. The first is the evaluation of a single production process to identify hotspots of concern that can be prioritized for action (e.g., substitution). The second one is the possibility, if needed, of developing comparison of multiple production processes to assess how stable the final scores of the CI-SSbDC are. Via the use of boxplots, the process developer can easily understand what the distribution of final scores of the CI-SSbDC for each production process is. This enables studying the robustness of the final decision recommendation.

CRediT authorship contribution statement

Ana Arias: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis. **Marco Cinelli:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Maria Teresa Moreira:** Writing – review & editing, Supervision. **Stefano Cucurachi:** Writing – review & editing, Supervision, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interest or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.spc.2024.09.027.

References

Abbate, E., Garmendia Aguirre, I., Bracalente, G., Mancini, L., Tosches, D., Rasmussen, K., Bennett, M.J., Rauscher, H., Sala, S., 2024. Safe and Sustainable by Design Chemicals and Materials - Methodological Guidance. Publications Office of the European Union, Luxembourg. https://doi.org/10.2760/28450, JRC138035.

Ali, S.S., Elsamahy, T., Abdelkarim, E.A., Al-Tohamy, R., Kornaros, M., Ruiz, H.A., Sun, J., 2022. Biowastes for biodegradable bioplastics production and end-of-life scenarios in circular bioeconomy and biorefinery concept. Bioresour. Technol. 363, 127869. https://doi.org/10.1016/j.biortech.2022.127869.

Apel, C., Sudheshwar, A., Kümmerer, K., Nowack, B., Midander, K., Strömberg, E., Soeteman-Hernández, L.G., 2024. Safe-and-sustainable-by-design roadmap: identifying research, competencies, and knowledge sharing needs. RSC Sustainability. https://doi.org/10.1039/D4SU00310A.

Arias, A., Feijoo, G., Moreira, M.T., 2021a. Process and environmental simulation in the validation of the biotechnological production of nisin from waste. Biochem. Eng. J. 174, 108105. https://doi.org/10.1016/j.bej.2021.108105.

Arias, A., Feijoo, G., Moreira, M.T., 2021b. Establishing the multi-criteria roadmap and metrics for the evaluation of active films for food packaging. Current Research in Green and Sustainable Chemistry 4, 100160. https://doi.org/10.1016/j.crgsc.2021.100160.

Bottero, M., Ferretti, V., Mondini, G., 2014. Constructing multi-attribute value functions for sustainability assessment of urban projects. In: Computational Science and Its Applications–ICCSA 2014: 14th International Conference, Guimarães, Portugal, June 30–July 3, 2014, Proceedings, Part III 14. Springer International Publishing, pp. 51–64. https://doi.org/10.1007/978-3-319-09150-1_5.

Caldeira, C., Farcal, L., Garmendia Aguirre, I., Mancini, L., Tosches, D., Amelio, A., Rasmussen, K., Rauscher, H., Riego Sintes, J., Sala, S., 2022a. Safe and Sustainable by Design Chemicals and Materials – Framework for the Definition of Criteria and Evaluation Procedure for Chemicals and Materials. Publications Office of the European Union. https://doi.org/10.2760/487955 (JRC128591).

Caldeira, C., Farcal, R., Moretti, C., Mancini, L., Rauscher, H., Rasmussen, K., Riego Sintes, J., Sala, S., 2022b. Safe and Sustainable by Design Chemicals and Materials – Review of Safety and Sustainability Dimensions, Aspects, Methods, Indicators, and Tools. Publications Office of the European Union. https://doi.org/10.2760/879069.

Caldeira, C., Garmendia Aguirre, I., Tosches, D., Mancini, L., Abbate, E., Farcal, R., Lipsa, D., Rasmussen, K., Rauscher, H., Riego Sintes, J., Sala, S., 2023. Safe and Sustainable by Design Chemicals and Materials. Application of the SSbD Framework to Case Studies. Publications Office of the European Union. https://doi.org/10.2760/329423 (JRC131878).

Campos-Guzmán, V., García-Cáscales, M.S., Espinosa, N., Urbina, A., 2019. Life Cycle Analysis with Multi-Criteria Decision Making: A review of approaches for the sustainability evaluation of renewable energy technologies. Renewable and Sustainable Energy Reviews 104, 343–366.

Carnesecchi, E., Mostrag, A., Ciacci, A., Roncaglioni, A., Tarkhov, A., Gibin, D., Sartori, L., Benfenati, E., Yang, C., Dorne, J.L., 2023. OpenFoodTox: EFSA's chemical hazards database, Zenodo. https://zenodo.org/records/8120114. Also available at: https://www.efsa.europa.eu/en/microstrategy/openfoodtox.

Chipangamate, N.S., Nwaila, G.T., 2023. Assessment of challenges and strategies for driving energy transitions in emerging markets: a socio-technological systems perspective. Energy Geoscience, 100257. https://doi.org/10.1016/j.engeos.2023.100257.

Cinelli, M., Spada, M., Kim, W., Zhang, Y., Burgherr, P., 2021. MCDA Index Tool: an interactive software to develop indices and rankings. Environ. Syst. Decis. 41, 82–109. https://doi.org/10.1007/s10669-020-09784-x.

Cinelli, M., Kadziński, M., Miebs, G., Gonzalez, M., Słowiński, R., 2022a. Recommending multiple criteria decision analysis methods with a new taxonomy-based decision support system. Eur. J. Oper. Res. 302, 633–651. https://doi.org/10.1016/j.ejor.2022.01.011.

Cinelli, M., Burgherr, P., Kadziński, M., Słowiński, R., 2022b. Proper and improper uses of MCDA methods in energy systems analysis. Decis. Support. Syst. 163, 113848. https://doi.org/10.1016/j.dss.2022.113848.

Dias, L.C., Caldeira, C., Sala, S., 2024. Multiple criteria decision analysis to support the design of safe and sustainable chemicals and materials. Sci. Total Environ. 916, 169599. https://doi.org/10.1016/j.scitotenv.2023.169599.

Durlinger, B., Koukouna, E., Broekema, R., van Paassen, M., Scholten, J., 2017. Agri-footprint 3.0. Blonk Consultants, Gouda, the Netherlands.

European Commission, 2018. Directorate-General for Research and Innovation, Bioeconomy – The European Way to Use Our Natural Resources – Action Plan 2018. Publications Office. https://doi.org/10.2777/79401.

European Commission, 2021a. Commission Recommendation (EU) 2021/2279 of 15 December 2021 on the Use of the Environmental Footprint Methods to Measure and Communicate the Life Cycle Environmental Performance of Products and Organisations.

European Commission, 2021b. Directorate-General for Research and Innovation, European Green Deal – Research & Innovation Call. Publications Office of the European Union. https://doi.org/10.2777/33415.

European Commission, Regulation (EU) 2024/1252 of the European Parliament and of the Council of 11 April 2024 establishing a framework for ensuring a secure and sustainable supply of critical raw materials and amending Regulations (EU) No 168/2013, (EU) 2018/858, (EU) 2018/1724 and (EU) 2019/1020Text with EEA relevance.

European Commission, Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs, Grohol, M., Veeh, C., 2023. Study on the Critical Raw Materials for the EU 2023 – Final Report. Publications Office of the European Union. https://doi.org/10.2873/725585.

European-Commission, 2022. Commission Recommendation (EU) 2022/2510 of 8 December 2022 establishing a European assessment framework for 'safe and sustainable by design' chemicals and materials. Off. J. Eur. Union L 325/179.

Gautam, S., Das, D.B., Saxena, A.K., 2024. Economic indicators evaluation to study the feasibility of a solar agriculture farm: a case study. Solar Compass 10, 100074. https://doi.org/10.1016/j.solcom.2024.100074.

Greco, S., Ehrgott, M., Figueira, J., 2016. Multiple Criteria Decision Analysis: State of the Art Surveys. Springer-Verlag, New York. https://doi.org/10.1007/b100605.

Hristozov, D., Zabeo, A., Soeteman-Hernández, L.G., Pizzol, L., Stoycheva, S., 2023. Safe-and-sustainable-by-design chemicals and advanced materials: a paradigm shift towards prevention-based risk governance is needed. RSC Sustainability 1 (4), 838–846. https://doi.org/10.1039/D3SU00045A.

Huijbregts, M.A., Steinmann, Z.J., Elshout, P.M., Stam, G., Verones, F., Vieira, M., Zijp, M., Hollander, A., Van Zelm, R., 2017. ReCiPe2016: a harmonised life cycle impact assessment method at midpoint and endpoint level. Int. J. Life Cycle Assess. 22, 138–147. https://doi.org/10.1007/s11367-016-1246-y.

Ioannidou, S.M., Stylianou, E., Pateraki, C., Kookos, I., Rabaey, K., Koutinas, A., Ladakis, D., 2023. Techno-economic and environmental sustainability assessment of succinic acid production from municipal biowaste using an electrochemical membrane bioreactor. Chem. Eng. J. 473, 145070. https://doi.org/10.1016/j.cej.2023.145070.

Keeney, R.L., 2020. Give Yourself a Nudge: Helping Smart People Make Smarter Personal and Business Decisions. Cambridge University Press, Cambridge. https://doi.org/10.1017/9781108776707.

Keeney, L.R., Raiffa, H., 1976. Decisions With Multiple Objectives: Preferences and Value Tradeoffs. Wiley, New York. https://doi.org/10.1017/CBO9781139174084.

Kiran, D.R., 2022. Chapter twenty-two-machinery replacement analysis. In: Principles of Economics and Management for Manufacturing Engineering, pp. 259–267. https://doi.org/10.1016/B978-0-323-99862-8.00002-9.

Kobayashi, Y., Peters, G.M., Ashbolt, N.J., Shiels, S., Khan, S.J., 2015a. Assessing burden of disease as disability adjusted life years in life cycle assessment. Sci. Total Environ. 530, 120–128. https://doi.org/10.1016/j.scitotenv.2015.05.017.

Kobayashi, Y., Peters, G.M., Ashbolt, N.J., Heimersson, S., Svanström, M., Khan, S.J., 2015b. Global and local health burden trade-off through the hybridisation of quantitative microbial risk assessment and life cycle assessment to aid water management. Water Res. 79, 26–38. https://doi.org/10.1016/j.watres.2015.03.015.

Langhans, S.D., Lienert, J., 2016. Four common simplifications of multi-criteria decision analysis do not hold for river rehabilitation. PLoS One 11, e0150695. https://doi.org/10.1371/journal.pone.0150695.

Langhans, S.D., Lienert, J., Schuwirth, N., Reichert, P., 2013. How to make river assessments comparable: a demonstration for hydromorphology. Ecol. Indic. 32, 264–275. https://doi.org/10.1016/j.ecolind.2013.03.027.

Langhans, S.D., Reichert, P., Schuwirth, N., 2014. The method matters: a guide for indicator aggregation in ecological assessments. Ecol. Indic. 45, 494–507. https://doi.org/10.1016/j.ecolind.2014.05.014.

Leipold, S., Petit-Boix, A., 2018. The circular economy and the bio-based sector-perspectives of European and German stakeholders. J. Clean. Prod. 201, 1125–1137. https://doi.org/10.1016/j.jclepro.2018.08.019.

Lindfors, A., 2021. Assessing sustainability with multi-criteria methods: a methodologically focused literature review. Environmental and Sustainability Indicators 12, 100149. https://doi.org/10.1016/j.indic.2021.100149.

Ma, W.J., Husain, M., Bays, P.M., 2014. Changing concepts of working memory. Nat. Neurosci. 17 (3), 347–356. https://doi.org/10.1038/nn.3655.

Martinez-Hernandez, E., Ramírez-Verduzco, L.F., Amezcua-Allieri, M.A., Aburto, J., 2019. Process simulation and techno-economic analysis of bio-jet fuel and green diesel production—minimum selling prices. Chem. Eng. Res. Des. 146, 60–70. https://doi.org/10.1016/j.cherd.2019.03.042.

Ministry of Infrastructure and water management, Government of The Netherlands, 2024. Redesigning Chemical Innovation - Essays on Safe and Sustainable by Design.

Nardo, M., Saisana, M., Saltelli, A., Tarantola, S., Hoffman, A., Giovannini, E., 2008. Handbook on Constructing Composite Indicators. Methdology and User Guide. OECD, Paris. https://doi.org/10.1787/18152031.

Opon, J., Henry, M., 2020. A multicriteria analytical framework for sustainability evaluation under methodological uncertainties. Environ. Impact Assess. Rev. 83, 106403. https://doi.org/10.1016/j.eiar.2020.106403.

OSHA. Occupational Safety and Health Administration, U.S. Department of Labor, 2024. Occupational Chemical Database. Available at: https://www.osha.gov/chemicaldata.

Paas, F., Tuovinen, J.E., Tabbers, H., Van Gerven, P.W.M., 2003. Cognitive load measurement as a means to advance cognitive load theory. Educ. Psychol. 38 (1), 63–71. https://doi.org/10.1207/S15326985EP3801_8.

Pan, S., Zabed, H.M., Zhao, M., Qi, X., Wei, Y., 2023. Techno-economic and life cycle assessments for bioenergy recovery from acid-hydrolyzed residues of sugarcane bagasse in the biobased xylose production platform. J. Clean. Prod. 400, 136718. https://doi.org/10.1016/j.jclepro.2023.136718.

PARC SSbD Toolbox version 0.1 Guidebook, 2024. Partnership for the assessment of risks from chemicals. https://www.parc-ssbd.eu/wp-content/uploads/2024/06/SSbD-toolbox-guidebook-v2.0-1.pdf.

Piccinno, F., Hischier, R., Seeger, S., Som, C., 2018. Predicting the environmental impact of a future nanocellulose production at industrial scale: application of the life cycle assessment scale-up framework. J. Clean. Prod. 174, 283–295. https://doi.org/10.1016/j.jclepro.2017.10.226.

Pinto, J., Barroso, T., Capitao-Mor, J., Aguiar-Ricardo, A., 2020. Towards a new, green and dynamic scoring tool, G2, to evaluate products and processes. J. Clean. Prod. 276, 123079. https://doi.org/10.1016/j.jclepro.2020.123079.

Radebe, N., Chipangamate, N., 2024. Mining industry risks, and future critical minerals and metals supply chain resilience in emerging markets. Res. Policy 91 (C). https://doi.org/10.1016/j.resourpol.2024.104887.

Rajendran, N., Runge, T., Bergman, R.D., Nepal, P., Houtman, C., 2023. Techno-economic analysis and life cycle assessment of cellulose nanocrystals production from wood pulp. Bioresour. Technol. 377, 128955. https://doi.org/10.1016/j.biortech.2023.128955.

Reichert, P., Langhans, S.D., Lienert, J., Schuwirth, N., 2015. The conceptual foundation of environmental decision support. J. Environ. Manag. 154, 316–332. https://doi.org/10.1016/j.jenvman.2015.01.053.

Reins, L., Wijns, J., 2024. The "safe and sustainable by design" concept–a regulatory approach for a more sustainable circular economy in the European Union? European Journal of Risk Regulation 1–18.

Saling, P., Valdivia, S., Sonnemann, G., 2024. Chapter 20: sustainability assessments of chemical products. In: Handbook on Life Cycle Sustainability Assessment. Edward Elgar Publishing, pp. 279–289. https://doi.org/10.4337/9781800378650.00031.

de Souza, N.R.D., Matt, L., Sedrik, R., Vares, L., Cherubini, F., 2023. Integrating ex-ante and prospective life-cycle assessment for advancing the environmental impact analysis of emerging bio-based technologies. Sustainable Production and Consumption 43, 319–332. https://doi.org/10.1016/j.spc.2023.11.002.

Stegmann, P., Londo, M., Junginger, M., 2020. The circular bioeconomy: its elements and role in European bioeconomy clusters. Resources, Conservation & Recycling: X 6, 100029. https://doi.org/10.1016/j.rcrx.2019.100029.

Sudheshwar, A., Apel, C., Kümmerer, K., Wang, Z., Soeteman-Hernández, L.G., Valsami-Jones, E., Nowack, B., 2024. Learning from Safe-by-Design for Safe-and-Sustainable-by-Design: Mapping the current landscape of Safe-by-Design reviews, case studies, and frameworks. Environment International 183, 108305.ISO 690.

Sustainability, Pré, 2020. SimaPro Database Manual: Methods Library. Amersfoort, The Netherlands, Pré Sustainability, p. 98.

Tavares, T.D., Ribeiro, A.R., Silva, C., Antunes, J.C., Felgueiras, H.P., 2023. Combinatory effect of nisin antimicrobial peptide with bioactive molecules: a review. Journal of Drug Delivery Science and Technology, 105246. https://doi.org/10.1016/j.jddst.2023.105246.

Thies, C., Kieckhäfer, K., Spengler, T.S., Sodhi, M.S., 2019. Operations research for sustainability assessment of products: a review. Eur. J. Oper. Res. 274, 1–21. https://doi.org/10.1016/j.ejor.2018.04.039.

US National Library of Medicine''s (NLM) Toxicology Data Network, 2024. The Hazardous Substances Data Bank (HSDB®). Available at: http://wayback.archive-it.org/org-350/20180125173245/https://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm.

Wątróbski, J., Jankowski, J., Ziemba, P., Karczmarczyk, A., Zioło, M., 2019. Generalised framework for multi-criteria method selection. Omega 86, 107–124. https://doi.org/10.1016/j.omega.2018.07.004.

Wernet, G., Bauer, C., Steubing, B., Reinhard, J., Moreno-Ruiz, E., Weidema, B., 2016. The ecoinvent database version 3 (part I): overview and methodology. Int. J. Life Cycle Assess. 21, 1218–1230. https://doi.org/10.1007/s11367-016-1087-8.

Wilson, M.C., Wu, J., 2017. The problems of weak sustainability and associated indicators. Int. J. Sustain. Dev. World Ecol. 24 (1), 44–51. https://doi.org/10.1080/13504509.2015.1136360.

Yadav, D., Rangabhashiyam, S., Verma, P., Singh, P., Devi, P., Kumar, P., Kumar, K.S., 2021. Environmental and health impacts of contaminants of emerging concerns: recent treatment challenges and approaches. Chemosphere 272, 129492. https://doi.org/10.1016/j.chemosphere.2020.129492.

Zanghelini, G.M., Cherubini, E., Soares, S.R., 2018. How Multi-Criteria Decision Analysis (MCDA) is aiding Life Cycle Assessment (LCA) in results interpretation. J. Clean. Prod. 172, 609–622. https://doi.org/10.1016/j.jclepro.2017.10.230.

Zappe, A.L., de Oliveira, P.F., Boettcher, R., Rodriguez, A.L., Machado, Ê.L., Dos Santos, P.A.M., Rodriguez-Lopez, D.A., de Matos, M.A.A., 2020. Human health risk and potential environmental damage of organic and conventional Nicotiana tobaccum production. Environ. Pollut. 266, 114820. https://doi.org/10.1016/j.envpol.2020.114820.

Žižlavský, O., 2014. Net present value approach: method for economic assessment of innovation projects. Procedia Soc. Behav. Sci. 156, 506–512. https://doi.org/10.1016/j.sbspro.2014.11.230.