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Safe and sustainable chemicals and materials: a review of sustainability assessment frameworks†

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In the context of the EU Chemicals Strategy for Sustainability, a key action regards the development of a framework to identify criteria for safe and sustainable by design chemicals and materials. The integration of safety and sustainability considerations is challenging, and this systematic review investigates how aspects pertaining to sustainability have been implemented in 155 frameworks proposed by scholars, industry, governments and non-governmental organizations. In particular, this review scrutinizes methods, models and indicators for environmental, social and economic aspects in frameworks combining multiple sustainability dimensions. Furthermore, the application of such frameworks to an early stage of chemicals and materials development was also analysed. The review unveiled that the majority of the frameworks are purely conceptual/theoretical, while some attempts are made by others towards providing methods and indicators for the assessment as well as operational procedure of decision support. Life cycle considerations are often remarked as necessary for evaluating the environmental sustainability of chemicals, climate change being the environmental impact mentioned by the majority of frameworks. Social sustainability aspects with quantitative indicators have been proposed only in a few studies so far. Another aspect often disregarded is data uncertainty. Although the reviewed frameworks showed several similarities in structure and aspects covered, indicators often differ significantly. Hence, using one framework instead of another might lead to a different outcome.

1. Introduction

The chemicals sector contributes to 7% of the global climate change impact and 10% of the global energy demand.[1,2] Given the growing consumption of chemicals, the concern about their environmental, health, and social impacts has significantly grown.[2–4]

A key policy goal defined in the European Green Deal is a zero pollution/toxic-free environment, together with climate neutrality, biodiversity protection, and circular economy.[5] To support such ambition, the EU Chemicals Strategy for Sustainability (CSS) – Towards a Toxic-Free Environment puts forward actions to reduce impacts on human health and the environment associated with chemicals, materials, products, and services.[6] In particular, the EU CSS calls for the definition of criteria for Safe and Sustainable by Design (SSbD) chemicals and materials by integrating safety, circularity and functionality, minimizing their life cycle environmental footprint.

The selection of safer alternatives has been the subject of several studies proposing frameworks for the assessment.[7–9] Following these frameworks, viable or new alternatives are screened before commercialization to avoid regrettable substitutions. These frameworks include a hazard and risk assessment[10–13] focusing mostly on the physicochemical properties (*e.g.* flammability), human toxicity (*e.g.* carcinogenicity) and ecotoxicity (*e.g.* bioaccumulation) of chemicals and materials. Within the European Union, environmental, health, and safety (EHS) legislation criteria are set by the REACH regulation.[14]

A seminal approach to considering sustainability aspects in chemical development was proposed in the field of green chemistry. The Green Chemistry concept was introduced in the environmental protection strategy of the U.S. (United States) Environmental Protection Agency (EPA) in the early 1990s.[15] This concept then became well known with the publication of the 12 Green Chemistry principles by Anastas and Warner[16] which consider efficient utilization of raw materials and elimination of waste and toxic and/or hazardous substances.[17]

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In the past decade, the integration of sustainability aspects in the selection of chemicals and materials has been gaining prominence with the ambition of moving towards safer and more sustainable chemicals and materials.[9,18–22] Incorporating chemicals' sustainability aspects besides safety allows accounting for trade-offs between exposure of humans and ecosystems and environmental impacts (*e.g.* climate change) associated with chemical production and supply chains.

To gain insights into which safety and sustainability aspects would be relevant to be included in a framework for the development of SSbD criteria for chemicals and materials, the European Commission Joint Research Centre (EC-JRC) carried out an initial review on how sustainability aspects have been implemented in decision frameworks for safety, identifying which dimensions, aspects, methods and indicators have been proposed, as well as the decision approaches applied in the overall sustainability assessment framework.[23] This review informed the development of the SSbD framework by the EC-JRC[24] that underpins the EC Recommendation establishing a European assessment framework for safe and sustainable by design chemicals and materials.[25] The framework considers the Green Chemistry principles key to design SSbD chemicals but their performance should be assessed by means of comprehensive sustainability assessment that considers the entire life cycle. A testing period by stakeholders is taking place and the revision of the framework built based on the feedback obtained during this period is foreseen. To inform the further development of the EC framework, a more systematic analysis of the frameworks is needed, especially unveiling the key scientific underpinning of the proposed framework, their level of operationalization and the focus to design support *versus* a proper and comprehensive assessment of the alternatives. Hence, this study aims to investigate indicators with respective methods covering sustainability aspects in frameworks integrating multiple sustainability dimensions and discuss the level of integration reached so far, highlighting frameworks used for the design of chemicals and materials, including in the early stage of development.

2. Materials and methods

A systematic procedure to select frameworks to be included in the review (section 2.1) is illustrated and the aims and structure of the review (section 2.2) presented, including the classification of the different sustainability aspects analysed (section 2.3).

2.1 Selection of the frameworks to be reviewed

This review scrutinized frameworks from different sources and proposed by different types of stakeholders. Hence, the frameworks were identified from scientific articles, grey literature and regulations. In this context, the term "framework" refers to any decision structure made of aspects and indicators to proceed from the relevant data to the outcome to inform future actions and support decision making. For example, a so-called framework can represent the decision structure implemented in chemical design tools.

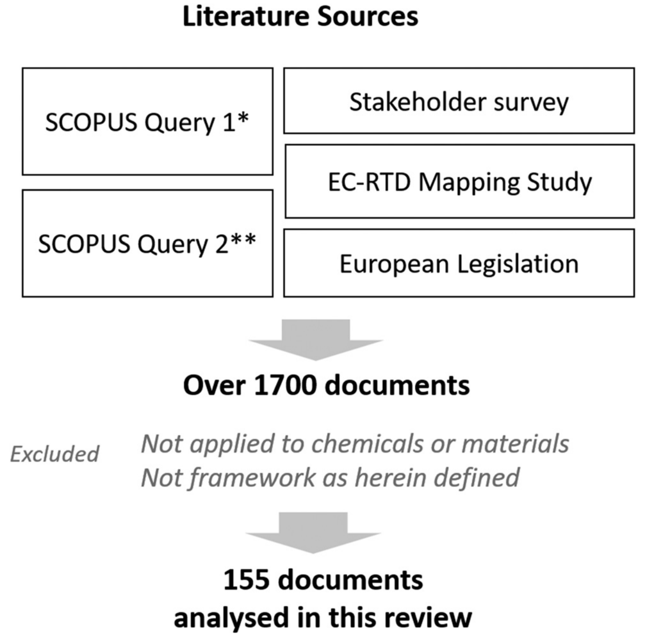

Fig. 1 Sources for the frameworks considered in this review. *as in Caldeira *et al.*[23] updated to May 2023. **new query considered for this review.

An overview of sources used to perform this review is presented in Fig. 1. The review builds and expands on the review carried out by the EC-JRC,[23] the EC-RTD mapping study[26] and the results of a targeted stakeholders' survey.[27] The latter provided information mainly on grey literature and existing legislation that considers sustainability aspects.

Moreover, the scientific literature obtained from the Scopus database with query 1 characterized by terms linked to the concept of safe and sustainable chemicals§ was updated in May 2023 including 868 articles. The search string used in Scopus was characterised also by the terms "solvent", "selection" and "guide" since solvent selection guides reporting alternative assessment frameworks for solvent selection have been used for more than 20 years in the pharmaceutical sector,[28] making this term well established. Moreover, since multi criteria decision analysis (MCDA) has been highlighted as a key instrument for sustainability assessment in general, as discussed in major works and reviews (*e.g.* ref. 29 and 30)

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§ TITLE-ABS-KEY (("alternatives assessment" OR "chemicals alternative assessments" OR "alternatives analysis" OR "substitution assessment" OR "chemicals assessment" OR "solvent selection" OR "solvents selection" OR "solvent design" OR "safe and sustainable" OR "social LCA" OR "life cycle costing" OR "life cycle cost") AND ("chemical" OR "chemicals" OR "solvent" OR "solvents") AND ("framework" OR "frameworks" OR "guide" OR "guides" OR "methodology" OR "methodologies" OR "tool" OR "tools")).

an additional search in the Scopus database with query 2¶ was done, returning over 1400 results.

Once duplicates (studies captured in both reviews) were eliminated, the abstracts were revised. Those dealing with topics not related to chemicals and materials *e.g.* in supply chain management (*e.g.*, supplier selection, transportation, location) and waste management (recycling, materials recovery, remediation) were excluded. The main text was considered in cases when reading the abstract and the title was not sufficient for such a screening. Additional frameworks not found directly by the Scopus search but cited by excluded case studies or reviews were also included in our analysis. In the end, 155 documents were considered in this review.

2.2 Aim and structure of the review

The main aim of this review is to update and extend the review carried out by Caldeira *et al.*[23] to inform the further development of the EC SSbD framework and to analyse to which extent the frameworks have been applied in the early stage of development of chemicals and materials. Therefore, frameworks introduced and adopted for chemicals and materials in the design phase were pinpointed to identify potential indicators used for sustainability assessment in the early stage of development. The following elements were collected and analysed in all the selected frameworks:

i. Coverage of sustainability dimensions (*i.e.* safety, environmental, social, and economic) and aspects (*e.g.* climate change) as well as which indicators and respective methods are suggested.

ii. Adoption of a life cycle approach and if so, what is the methodology and which are the environmental impacts considered. As mentioned in the Introduction, the EU CSS[31] recalls the importance of a life cycle perspective in minimizing chemicals' potential impacts to detect shifts in burdens between impact categories, life cycle stages or geographic locations.

iii. Decision support procedure implemented, including eventual scoring systems and the level of aggregation of the evaluation outcome as well as how data gaps and uncertainty were taken into account in the assessment.

2.3 Classification of the aspects considered in the reviewed frameworks

The aspects considered by the reviewed frameworks were classified into four categories as in Caldeira *et al.*:[23]

2.3.1. Resource, processing- and product-related aspects. Aspects related to the chemical/material production process *e.g.* efficiencies related to energy or chemical reactions, type of feedstock, *etc.* or products *e.g.* recycled content or durability; the aspects belonging to this level are often linked to pressures on multiple sustainability dimensions;

2.3.2. Pressure aspects. Aspects reflecting various pressures along the value chain such as emissions to water, soil or air, operational costs, working hours, *etc.*

2.3.3. Impact aspects. Aspects reflecting the effect *i.e.* the impacts (environmental, social, and economic) caused by resource and processing- and product-related aspects and by the pressure aspects. In the case of social and economic aspects, however, the assessment is usually limited to performance indicators, as clear impact pathways and impact assessment methods are not always available.[32]

3. Frameworks for sustainability assessment of chemicals and materials

From the literature collected, 155 frameworks were selected to be analysed in detail as presented in the following sections. Section 3.1 provides an overview of the frameworks whilst section 3.2 provides detailed information on dimensions, aspects, and indicators. The consideration of life cycle approaches is discussed in section 3.3, the evaluation procedure adopted in section 3.4 and how data gaps and uncertainty were considered in section 3.5.

3.1 Overview of the frameworks analysed

Table 1 presents an overview of the frameworks regarding the field of application *i.e.* if it was applied to chemicals,|| materials,** or products,†† life cycle considerations, application in the early stage of development, decision procedure, uncertainty consideration and the stakeholder who developed the approaches (*e.g.* academia or industry). Most of the frameworks focused on chemicals[89] and materials,[43] and less on products.[20] 105 frameworks considered life cycle approaches, and 81 included the decision procedure in their analysis. Fewer frameworks included uncertainty.[25] Out of 155 frameworks, 102 were proposed by academia, 15 by certification schemes and 14 by industry. Eight frameworks for chemicals were proposed (or coordinated) by governmental agencies such as the European Environmental Agency[33] and the German Federal Environment Agency,[34] in Europe and the US National Research Council[35] and the USA-based Interstate Chemicals Clearinghouse[36] in USA. The 6 frameworks proposed by international organizations are designed for chemicals in general,[37–40] plastics,[41] nanomaterials[42] and electronics.[43] The

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¶ TITLE-ABS-KEY (multicriteria OR multi-criteria OR "multiple criteria" OR mcda OR mcdm OR multiattribute) AND (chemical OR material OR substance) AND (safe* or sustainab*).

|| Chemicals are substances and mixtures as defined in Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) and Classification, Labelling and Packaging (CLP) legislations.

** Materials denote either substances or mixtures which may or may not yet fulfil the definition of an article under REACH and may be of natural or synthetic origin.[24]

†† Products are goods supplied for distribution, consumption or use on the Community market whether in return for payment or free of charge (EU Ecolabel). Materials denote either substances or mixtures which may or may not yet fulfil the definition of an article under REACH and may be of natural or synthetic origin.[24]

Table 1 Overview of the literature review regarding the consideration of the life cycle, application in the early stage of development, the decision procedure in place, the consideration of uncertainty and the type of document

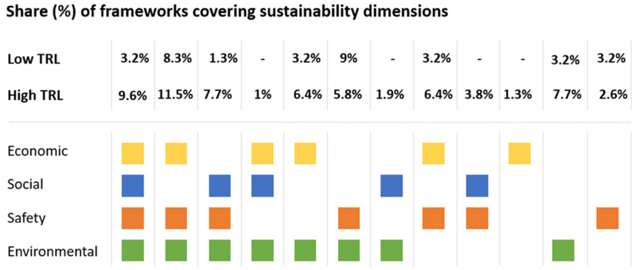
Scope of the application	Total of frameworks	Life cycle consideration	Early stage application	Decision procedure	Uncertainty
Chemicals	**89**	**59**	**35**	**48**	**12**
Drug	1			★ 1	
Energy retardants	1			★ 1	★ 1
Flame retardants	3	★ 2	★ 2	★ 1	
Fluorinated greenhouse gases (F-gases)	1	■ 1			
Fragrance	2	★ ▲ 2	★ 1	★ 1	
Fuels	8	★ 3	★ 2	★ 8	★ 3
Metals	1	★ 1		★ 1	★ 1
Polymers	1	★ 1		★ 1	
Precursor	2	★ 2	★ 2	★ 2	
Solvents	33	★ 16	★ 16	★ 18	★ 5
Surfactant	1	★ 1		★ 1	
Not specified	35	● ★ 30	● ★ 12	★ 13	◆ 2
Materials	**43**	**30**	**13**	**29**	**11**
Additive manufacturing	1	★ 1		★ 1	
Bioplastics	1	★ 1	★ 1		
Bulding materials	18	▲ ★ 11	★ 7	★ 17	★ 8
Carbon fiber	1	★ 1			
Compositers	1	★ 1		1	
Nanomaterials	3	★ 5	★ 3	1	★ 1
Plastics	4	★ ▲ ● 5	★ 1	★ 1	
Protective membrane	1		★ 1	★ 1	★ 1
Textiles	4	▲ 1			
Vehicle (carrier)	2	★ 1		★ 2	
Not specified	6	★ 3		★ 5	★ 1
Products	**20**	**14**	**1**	**4**	**1**
Batteries	1	★ 1			
Chemical industry	1	★ 1		★ 1	
Cosmetics	1		★ 1	★ 1	
Electronics	2	▲ 2			
Energy	2	■ ★ 2			
Financial	1	■ 1			
IT	1				
Not specified	11	■ ◆ ● ▲ 7		● 2	● 1
Chemicals and materials	1	★ 1	★ 1		
Chemical and products	1				
Materials and products	1	▲ 1			

certification;	▲
guidance;	●
regulation;	■
scientific paper; and	★
tool.	◆

4 frameworks from NGOs were developed for chemicals[44–47] and electronics.[48]

Fig. 2 depicts the dimensions covered *i.e.* safety, and environmental, economic, and social sustainability. Despite this division, the authors recognize that safety is integrated in sustainability: it is important to note that safety is a wide concept embedded in several Sustainable Developments Goals, and chemical safety is stated in several targets relating to human health, environmental quality, and access to services and resources. However, since the SSbD concept distinguishes the two terms (safety and sustainability), the same was done in this work.

Most of the frameworks consider environmental and economic aspects[47] or only environmental.[37] A lower number of frameworks consider social aspects that are either combined with environmental aspects[7] or with environmental and economic.[20] For the latter in which environmental, economic and social aspects are considered there are frameworks suggested for example in ref. 34, 36, 39 and 49–54.



Share (%) of frameworks covering sustainability dimensions

Low TRL	3.2%	8.3%	1.3%	-	3.2%	9%	-	3.2%	-	-	3.2%	3.2%
High TRL	9.6%	11.5%	7.7%	1%	6.4%	5.8%	1.9%	6.4%	3.8%	1.3%	7.7%	2.6%
Economic	🟨	🟨		🟨	🟨			🟨		🟨		
Social	🟦		🟦	🟦			🟦		🟦			
Safety	🟧	🟧	🟧			🟧		🟧	🟧			🟧
Environmental	🟩	🟩	🟩	🟩	🟩	🟩	🟩				🟩	

Fig. 2 Aspects covered by the literature for frameworks applied at low TRLs and developed products.

The work by Rossi *et al.*[53] is a seminal framework to guide alternative assessment of chemicals, materials, and products. The evaluation performed *via* this framework look at four major areas: (1) impacts on human health and the environment, (2) social justice impacts, (3) technical performance and (4) economic feasibility. The framework proposed by the German Environmental Agency (UBA) investigates potential impacts of chemicals on human health and the environment and on social responsibilities in supply chains,[34] while economic aspects are addressed to a minor extent only. The framework proposed by CEFIC (European Chemical Industry Council) is comprehensive in terms of covered dimensions but it is still at a conceptual level. The framework from the World Business Council on Sustainable Development (WBCSD) regards the Chemical Industry Methodology for Portfolio Sustainability Assessments (PSA).[55] This framework is built on two established guidance documents on assessing environmental and social impacts of chemical products based on a life cycle approach.[56,57] This framework is a major reference for frameworks further developed by companies implementing in-house PSA methodologies.[51,54,58] The framework proposed by the Interstate Chemicals Clearinghouse (IC2) includes considerations of the full life cycle of the product. Both environmental and social impacts are considered *via* a set of modules. A priority is given on the modules regarding hazard, cost, availability, performance evaluation, and exposure assessment – whilst others (Materials Management, Social Impact, and Life Cycle) should be considered if relevant to the particular chemical, product, or process under assessment. The Cradle to Cradle Certified® Product Standard presents a list of requirements that products should comply with, ranging from human health to product circularity, climate protection, and social fairness. It also includes water and soil stewardship, general requirements and recommendation for packaging.

A different distribution of the dimensions included has been observed for the frameworks that take the early stage of development into account. Fig. 2 clearly shows the low percentage of frameworks applied in the early stage of development analysing social aspects. Conversely, the economic aspect is covered by 53% of these frameworks, a percentage that drops to 32% for frameworks that do not focus on the design phase. This suggests the central role of economic aspects when dealing with new chemicals or materials in order to assess further efforts in the development of the chemical/material under consideration. A similar trend can be observed for frameworks dealing with the environmental aspect, which is included in the majority of frameworks (around 80%), both those considering the early stage of development and those not. Frameworks focusing on single sustainability dimensions were rarely identified, suggesting that frameworks covering more than one aspect are preferred as they provide a broader analysis.

3.2 Dimensions, aspects and indicators

Section 3.2.1 provides an overview of resource and processing- and product-related aspects. These aspects are not considered under any dimension in particular and they refer to the characteristics of the process or the final product that directly affect the amount and type of pressure and related impacts in multiple dimensions. Then, aspects related to environmental, social, and economic dimensions are presented in sections 3.2.2, 3.2.3, and 3.2.4, respectively. Detailed information collected for each framework is presented in the excel file provided in the ESI.†

3.2.1 Aspects related to resource use, and processing- and product-related aspects. Resources and processing- and product-related aspects were further classified into four different groups:

i. energy, including energy consumption/efficiency of a process or over the life cycle;

ii. circularity, considering features linked to reducing, reusing, repairing, refurbishing, remanufacturing, and recycling options;

iii. biodegradability, referring to the capacity for biological degradation of organic materials by living organisms down to the base substances such as water, carbon dioxide, methane, basic elements and biomass; and

iv. aspects related to the type and quantity of resources used and efficiency of the production process.

The indicators suggested in the frameworks associated with each aspect are summarized in Table 2, highlighting indicators used in frameworks in the early stage of development. Definitions and assessment methods are reported in the ESI.† Most of the frameworks include indicators related to the type and quantity of resources used. Indicators on biodegradability are seldom used, however with a slightly higher percentage in the case of frameworks considering the design phase. In contrast, circularity is highly analysed.

Energy. The amount of energy consumed‡‡ by a process, product or system was one of the most proposed indicators (46 frameworks). Energy efficiency and cumulative energy demand were also frequently used (32 frameworks). Cumulative energy demand is a sum of both the direct and indirect energy used

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‡‡ Annex 10 of the guide proposed by the German Environment Agency[34] provides a comprehensive overview of the energy consumption of chemicals and materials. In this guide, "green chemicals" are chemicals consuming less than 10 MJ kg^{-1} during production, "yellow chemicals" between 10 and 100 MJ kg^{-1} and "red chemicals" more than 100 MJ kg^{-1}.

Table 2 Indicators for resource, and processing- and product-related aspects

Aspect Indicator	Number of frameworks adopted	Early stage application
Resource, and processing- and product-related	**375**	**149**
Energy	**87**	**38**
Cumulative energy demand [MJ]	17	12
Energy conservation [–]	2	
Energy consumption [kW h or MJ]	39	14
Energy efficiency [%]	17	4
Energy intensity [kW h kg^{-1} or MJ kg^{-1}]	2	1
Non-renewable resources with energy content [MJ]	1	
Number of (process) steps [–]	1	1
Primary energy demand [MJ]	1	1
Process carbon footprint	1	1
Process efficiency [%]	1	1
Reaction efficiency [%]	2	2
Recycling energy [E]	1	
Renewable resources with energy content [MJ]	1	
Stoichiometric factor	1	1
Circularity	**112**	**36**
Aqueous waste valorisation [E]	1	1
Boiling temperature [°C]	10	5
Disassembly/reparability design [E]	10	
Durability [years]	13	4
Durability of the building [years]	1	
Energy requirement for recycling [MJ kg^{-1}]	2	1
Heat of vaporisation [MJ kg^{-1}]	2	1
Number of carbon atoms [E]	1	
Percentage of reclaimed products and their packaging materials [%]	1	
Purity of recovered solvent [%]	2	1
Recyclable?[–]	12	3
Recyclability/circularity [–]	21	8
Recycled content [%]	12	1
Recycling efficiency/recovery rate [%]	9	4
Reuse rate/reusability [–]	4	2
Solvent selectivity [–]	2	
Used organic solvent valorisation [–]	1	1
Waste reduction [–]	1	13
Waste utilization [–]	5	3
Yield of extraction (%)	2	
Biodegradability	**19**	**7**
Biodegradability [–]	4	1
Biodegradability requirement [–]	6	
Biodegradability [–]	4	4
Marine biodegradability [–]	2	
Octanol–water distribution coefficient [Kow]	2	2
Soil biodegradability [–]	1	
Resources: types, quantity, and efficiency considerations	**157**	**68**
Amount of (solid/water) waste [kg or %]	17	4
Atom economy [%]	5	6
Biomass consumption [kg]	1	
Carbon economy [–]	1	1
E-factor [%]	6	4
Fossil fuel consumption [kg]	1	1
Global material economy [%]	1	1
Hazard Waste [kg]	2	1
Imported resources [E]	1	
Mass yield [%]	2	2
Material conservation [E]	2	
Material intensity index [%]	4	1
Net mass of materials consumed [kg]	6	4
Non-renewable resource amount [kg]	4	2
Non-hazardous waste [kg]	2	1
Number of solvents [E]	1	1
Raw material consumption [kg per ton]	2	2
Raw material origin [E]	2	2
Reaction efficiency [%]	10	5
Recycled input materials [%]	1	
Relative process greenness [–]	1	1
Renewability of resources [%]	5	5
Renewable or fossil? [–]	18	6
Renewable resource amount [kg]	4	2
Resource consumption [kg]	4	2
Resource efficiency	1	1
Resource valorisation [–]	2	2
Solid waste [kg per ton]	2	1
Solid waste generation [kg]	5	2
Solvent selectivity [–]	1	1
Use of critical raw materials?[–]	5	1
Waste characterisation potential [kg]	1	
Waste cleaning [–]	2	
Waste reduction algorithm [–]	1	1
Water consumption [m3]	32	7
Water efficiency [m3]	1	

throughout the life cycle. This indicator was often considered as a proxy for the increase or decrease of other environmental impacts that directly correlate with energy consumption such as climate change.[3,59–62] However, the correlation between these two indicators are expected to become lower in future scenarios, considering the ambition of achieving an energy mix relying less on fossil fuels.

Circularity. Circularity related indicators have been proposed in 58 of the reviewed frameworks, of which 24 were focused on the design phase. The indicators mostly refer to the recyclability for chemicals and durability and reparability for products, with a high variability on how the recyclability of a chemical or product is defined. Some conceptually report information on its recyclability,[30] while others[21] evaluate the recycled content or the recycling efficiency.

Various indicators measure the performance during distillation processes mostly found in frameworks applied to solvents as distillation is the major technique used by the chemical industries for recycling solvents.[63] These indicators were proposed in terms of amounts (*e.g.* the energy requirement for recycling), efficiencies (*e.g.* yield of extraction) or physical properties (*e.g.* boiling temperature). However, environmental trade-offs of recycling chemicals are overlooked using these indicators. For example, the energy needed for distillation to recover a solvent might be higher than producing it.[63]

To minimize undesirable trade-offs of circularity, two innovative approaches were proposed in ref. 2 and 64. Chavarrio *et al.*[64] proposed a quantitative multi-criteria decision method based on both the solvent and extraction processes under consideration. This method relies on criteria such as the cost of the solvent, yield of extraction, purity of recovered solvent, heat of vaporization, boiling temperature, solvent selectivity, *etc.* Wang and Hellweg[2] proposed a two-step circularity assessment to evaluate approaches to reduce the major causes of chemical losses and qualitatively catalogue chemicals into six major categories leading to different management practices for recovering the embedded raw materials. As pointed out by Wang and Hellweg,[2] most of the indicators used for assessing circularity are mass-based and can be misleading in guiding environmental sustainability. The authors give the example of lithium-ion batteries for which higher energy consumption and air pollution arises from current recycling technologies than from primary production. It is therefore essential to couple mass-based circularity indicators with methods that assess the environmental impacts of the 'circular' system.

Biodegradability. Non-biodegradable chemicals can persist in the environment for a long time, and they may become a hazard. For this reason, biodegradability was often considered as an aspect belonging to the safety dimension instead of the environmental dimension. Biodegradability as a hazard (persistence and bioaccumulation) is considered in legislation, guidelines and standards as well as in ecolabel criteria,[65] *e.g.* for lubricants[66] or cosmetics.[67]

As an environmental aspect, it was mostly qualitatively addressed. So, most frameworks mention biodegradability as an aspect causing environmental issues but not providing information on a specific indicator or method to be used. Indicators regarding biodegradability were often discussed with respect to the biodegradability of plastics based on specific standards *e.g.* ASTM D-6400[68] or the standard EN13432.[69] In particular, no life cycle-based indicator regarding plastic littering was found. In fact, modelling littering requires a wide range of data regarding fate, exposure and effect modelling, which are mostly unavailable *e.g.* data regarding degradation rates of additives, effects from ingestion of plastic particles, *etc.*[70] However, the LCA community is developing research in this field on the development of harmonized pathways to account for impacts of plastic litter, specifically to the marine environment.[71]

Type and quantity of resources and efficiency of the production process. Regarding the type of resource, the distinction between fossil and renewable feedstock is frequently proposed. Chemical production heavily relies on non-renewable resources as the input,[72] so the use of renewable resources instead of fossil ones to produce new chemicals is regarded as a possible way to improve chemicals' environmental sustainability (26 frameworks). A couple of frameworks developed by the pharmaceutical industry conceptualized this indicator in terms of the percentage of fossil feedstock over the total feedstock.[73,74] A more articulated indicator *via* multiple scores for the use of resources considering the availability of both renewable and non-renewable raw materials is proposed by the German Environment Agency.[34] However, similar to the mass-based indicators for circularity, the use of renewable feedstocks, such as biomass feedstock, can be misleading regarding environmental sustainability.

Water is the resource that most of the frameworks pointed out as a key aspect to consider, water consumption (m3) being the most recommended indicator at the pressure level (32 frameworks).

The amount of waste generated and the net mass of materials consumed were also recommended by 24 and 6 frameworks, respectively. The argument in favour of easy-to-calculate mass-based metrics measuring waste generation is often a proxy for the trends of most environmental impacts.[4,17] Indicators typically used in Green Chemistry such as atom economy and *E*-factor and similar mass-based metrics that can be expressed in terms of *E*-factors (*e.g.* mass intensity = *E*-factor + 1)[17] were also often proposed.

The idea behind mass-based metrics used in green chemistry is that the amount of waste generated is often a good proxy for all other environmental impacts.[4] However, this assumption would lead to misleading outcomes in other cases, such as environmental comparisons between fossil and bio-based alternatives.[17,22]

3.2.2 Environmental dimension.

This section presents the aspects related to the environmental dimension considered in the frameworks either at the pressure or impact level (Table 3). Environmental impacts caused by pressures can be quantified at two levels: at the midpoint level *i.e.* the direct consequence of the pressure and the endpoint level *i.e.* damage caused to

Table 3 Aspects under the environmental dimension at pressure and impact levels, including those used in the early stage of development

Aspect Indicator	Number of frameworks adopted	Early stage application
Environmental	**459**	**181**
Pressure		
Air emission	**25**	**12**
Air emissions	3	3
Atmospheric CO_2 emissions [g]	3	1
Atmospheric NO_X emissions [g]	5	2
Atmospheric SO_2 emissions [g]	3	1
Atmospheric VOC emissions [g]	2	
Critical air mass [%]	2	2
Dimethylformamide [g]	3	2
Fine particulate matter (mg PM 2.5)	4	1
Water emission	**18**	**13**
Biological oxygen demand 5 [g]	3	2
Chemical oxygen demand [g]	3	2
Contaminant emission [g]	1	
Critical water mass [%]	2	2
Total organic carbon [kg]	4	4
Water Discharge quality	2	
Water emissions [kg m^{-3}]	3	3
Soil emission	**1**	**1**
Soil emissions	1	1
Midpoint		
Toxicity	**61**	**25**
Bioconcentration factor	1	1
Ecotoxicity [CTU]	3	1
Ecotoxicity [–]	5	
Ecotoxicity damage [PDF m3d]	1	
Freshwater [eco]toxicity [CTUe]	4	3
Freshwater ecotoxicity [g $C_6H_4Cl_2$-eq]	5	2
Human toxicity – cancer potential [CTUh]	4	2
Human toxicity – no cancer potential [CTUh]	3	1
Human toxicity [–]	7	1
Human toxicity potential [kg 1,4 DCB eq or CTUh]	9	5
Indoor air quality [–]	1	
LCT human toxicity [mg intake]	3	1
Marine ecotoxicity [g $C_6H_4Cl_2$-eq]	3	2
Respiratory inorganics	1	1
Smog potential [kg NOx eq.]	1	
Terrestrial ecotoxicity [g $C_6H_4Cl_2$-eq]	10	5
Climate Change	**95**	**33**
C factor	1	
Climate change [–]	4	3
CO_2 balance	1	1
GWP 100 [kg CO_2eq]	89	29
Stratospheric ozone depletion	**26**	**12**
Ozone depletion [–]	1	1
Ozone depletion potential [kg CFC-11]	25	11
Particulate Matter	**10**	**5**
Particulate matter [PM2.5eq]	10	5
Ionizing radiation	**2**	**2**
Ionizing radiation [kBq U235 eq.]	2	2
Photochemical Ozone Formation	**29**	**15**
Photochemical oxidant formation and ecosystems [kg NOx-eq to air]	1	1
Photochemical oxidant formation and human health [kg NOx-eq to air]	1	1
Photochemical oxidation potential [PCO]	2	2
POCP [kg of ethene-eq or kg NMVOC or kg O3]	25	11
Acidification	**35**	**12**
Acidification potential [molc H + eq]	20	3
Aquatic acidification [kg H + ions]	1	1
Atmospheric acidification [kg SO_2eq]	2	2
Terrestrial acidification [kg SO_2eq]	12	6
Eutrophication	**36**	**14**
Eutrophication potential [kg of phosphate]	19	5
Freshwater eutrophication potential [kg P eq]	10	5
Marine eutrophication potential [mol N eq]	6	4
Terrestrial eutrophication potential [kg of N equivalents]	1	
Resources	**62**	**22**
Damage to Resources [–]	4	3
Eco-indicator 99 depletion of resources [–]	1	1
Fossil resource scarcity [kg oil eq.]	2	1
Land occupation [m^2a crop eq.]	8	3
Land requirements	1	
Land Usage [M ha]	1	
Land use [kg C deficit]	2	1
Land use [–]	5	
Limiting depletion of fossil/mineral resources [–]	4	2
Mineral resource scarcity [kg Cu eq.]	1	
Resource depletion potential [kg Sb eq.]	7	1
Resource use/depletion – fossil [MJ]	14	7
Water consumption potential [m^3eq]	1	1
Water depletion potential [m^3eq]	10	2
water footprints [m^3eq]	1	
Endpoint		
Air pollution – air pollution and acidification [DALY]	1	1
Biodiversity protection (conceptual)	10	1
Chemicals safety	2	1
Climate change damage [DALY]	2	
Air and water pollution [DALY]	1	
Eco-indicator 99 total [–]	8	2
Eco-indicator 99 ecosystem quality [–]	2	1
Eco-Indicator 99 human health [DALY]	2	1
Ecosystem quality (recipe)	3	2
Ecosystems (species year)	5	1
Ecosystem damage (conceptual)	2	
Embodied biodiversity footprints	1	
Human health (DALY)	8	2
Human health (recipe)	3	2
Influence/impact on public health	3	
Inherent safety indicator	1	
Ionizing radiation-human health [DALY]	1	
Oral toxicity [−log LD50]	1	1
Resource depletion [$]	3	

the ecosystem and human health. The latter is presented in Table 3 under "Integrated assessment".

Regarding indicators at the pressure level, NO_X, SO_2, CO_2 and fine particulate matter released into the air have been proposed as indicators in 3–4 frameworks. The indicator named the "critical air mass" index is an old environmental indicator proposed already in the nineties in chemicals' selection tools and early studies on green chemistry.[75,76] This indicator represents the mass of a specific type of air emissions (*e.g.* SO_2) emitted by a process over a standard value typically representing the maximum acceptable amount of that pollutant *e.g.* based on legislation requirements.

Critical water mass is analogous to the critical air mass indicator but for the water compartment.[75,76] Another indicator related to water emissions reported in the reviewed frameworks was the total organic carbon proposed to measure water pollution, especially by guides from the pharmaceutical industry.[73,74,77] This indicator refers to the total soluble and insoluble organic matter entering water bodies. Biological oxygen demand and chemical oxygen have been proposed by three frameworks each. These indicators are common indicators to measure water quality.[78] Finally, one indicator regarding soil emission was found at the pressure level mentioned by one framework.[79] Still, the indicator was just mentioned without providing further information. Besides "soil biodegradability" in the resource dimension, no other indicators to evaluate impacts on soil were found. Indicators linked to the soil impacts are "Terrestrial eutrophication potential", "Terrestrial ecotoxicity", and "Terrestrial acidification". This emphasizes the lack of interest in monitoring and assessing the impact on soils, focusing more attention on water and air emissions. In light also with the recent Proposal for a Directive on Soil Monitoring and Resilience,[80] there is a need to develop and include indicators representative of the soil compartments both at the pressure and impact levels in the future.

A particular indicator with a single occurrence[81] is a pressure-based indicator used as a proxy for toxicity in the EPA's GREENSCOPE (Gauging Reaction Effectiveness for the Environmental Sustainability of Chemistries with a multi-Objective Process Evaluator) tool. The definition of this indicator is detailed in Ruiz-Mercado *et al.*[82] Essentially, this indicator represents the ratio between the total mass of toxins released over the total mass of products.

Regarding the environmental impacts, there were numerous (slightly) different versions of mid-point level indicators covering the same aspect in the reviewed framework. Therefore, indicators were grouped with the closest indicator in the counting when reasonably connected to another one in the list. For example, if the acidification potential was reported with a missing unit or a slightly different name, it was counted as the same indicator.

As presented in Table 3, environmental impacts at the midpoint level in the reviewed frameworks relate to climate change, toxicity, pollution such as acidification, eutrophication, ozone depletion, photochemical ozone formation, particulate matter and ionizing radiation, and resources and *e.g.* land use or water depletion.

The most suggested indicator in the frameworks is by far the global warming potential.[89] This indicator represents the sum of Greenhouse Gas (GHG) emissions multiplied by the specific characterization factor. The calculation of this indicator depends on the time-scale, which was always 100 years in the reviewed frameworks reporting this indicator. The high occurrence of this indicator is due to both a broad acknowledgment of the priority of dealing with climate change and the scientific consensus on the model underpinning this indicator.[83] This indicator is also adopted in various EU policies, especially for energy and alternative fuels.[84,85]

Stratospheric ozone depletion potential is suggested in 25 frameworks. The calculation of this indicator is based on a steady-state ozone depletion potential model.[86] The indicator obtained from this characterization model represents the relative measure of the expected impact on ozone per unit mass emission of a gas compared to that expected from the same mass emission of CFC-11. The broad suggestion for this indicator reflects both consensuses on the methodology for its calculation and a broad scientific acknowledgment of the impact caused by the depletion of the ozone layer on humans (*e.g.* increased skin cancer cases) and plants. Substances causing ozone depletion have been listed in the Montreal Protocol on Substances that Deplete the Ozone Layer, which entered into force already on January 1, 1989.[87]

The photochemical oxidant formation potential, ozone depletion potential, eutrophication potential, and acidification potential were often suggested in the reviewed frameworks. Photochemical ozone formation directly or indirectly impacts human health *via* the generation of ozone at the ground level. To measure photochemical ozone formation impacts, photochemical ozone creation potential was suggested by two frameworks in the early stage of development. The LOTOS-EUROS[88] model is the most common method behind this indicator. Using this model, the photochemical ozone creation potential is determined by comparing the rate at which a unit mass of chemical reacts with a hydroxyl radical ($OH^{\bullet}$) to the rate at which a unit mass of ethylene reacts with OH.

The reviewed frameworks have frequently reported indicators for eutrophication and acidification impacts. These indicators are often considered when comparing bio-based and petrochemical alternatives.[70,89–93] In fact, eutrophication and acidification impacts are usually higher for bio-based alternatives than petrochemical ones. Eutrophication is due to the release of nutrients to soil or freshwater due to fuel combustion and fertilizers in agriculture. In aquatic compartments, such nutrient excess causes the growth of algae or other plants, limiting the development of the original ecosystem. Models for the calculation of eutrophication indicators can provide a single value with no distinction per compartment[94] or a separate result for freshwater and marine compartments[95] and terrestrial compartment.[96]

Available models for calculating acidification potentials usually refer to terrestrial acidification due to atmospheric deposition of acidifying compounds.[96] Terrestrial acidification is a global threat to plant diversity.[97] The most significant source of acidification is fuel combustion processes, especially for fuels with a high sulphur content as those used *e.g.* in tractors.

Regarding resources, the reviewed frameworks have often considered resource use/depletion – fossil (MJ), water depletion potential and land use indicators. For the depletion of fossil resources, the scarcity/resource depletion model in ref. 98 is implemented in most LCA midpoint methods. The same model can also provide an indicator for the depletion of metal and mineral resources suggested in 14 of the reviewed frameworks.

The method underpinning the water depletion potential indicator suggested by most frameworks is the Swiss Ecological Scarcity Method.[99] However, the AWARE model[100] has emerged more recently and it is currently recommended by the European Commission.[101] This model provides an indicator with the same unit as the Swiss Ecological Scarcity Method but with significantly different modelling of the characterization factors.

The indicators related to land use mentioned by the reviewed frameworks are based on various methods and models such as the Swiss Ecological Scarcity Method,[99] Ecoindicator 99,[102] the Soil Organic Matter model[103] and the LANCA model.[104] Also for land indicators, different models are not directly comparable even if the indicator might have the same unit since the characterization modelling often focuses on a different land-use aspect and covers different land types.

As also remarked as relevant by the EU CSS, various frameworks propose life cycle midpoint indicators for aspects typically considered in safety/risk assessments like ecotoxicity and human toxicity. The suggested indicators are based on various methods and models: the ReCiPe 2016 impact method,[95] the USEtox model,[105] the CML 2001 method[94] and EDIP97.[106] Indicators for toxicity aspects based on a different method/model provide significantly different results even when expressed for the same unit *e.g.* some do not consider certain compartments or do not consider acute (*i.e.* short-term) toxic effects in the ecotoxicity category.

Despite some LCA indicators for toxicity aspects being suggested by various frameworks, this should not lead to the thinking that LCA can replace risk assessments to evaluate whether a process is safe.[35] In fact, there is no direct equivalency between LCA toxicity-related midpoint impacts and outcomes from risk assessments. For example, LCA does not generally consider the direct exposure pathways from a product but through exposure in environmental media.[62] However, there are some attempts to bridge the gap between LCA and risk assessment.[107–110]

Another indicator proposed by various frameworks is particulate matter expressed in relative human health damage compared to fine particulate matter (PM 2.5 eq.) based on the model described by Rabl *et al.*[111]

Some of the frameworks suggest impacts at the endpoint level, based on damage-oriented modelling regarding three protection areas *i.e.*, human health, ecosystems and resources, *via* integrated assessments (Table 3). These indicators are mainly based on two impact assessment methods *i.e.*, ReCiPe 2016 (or earlier 2008 version) and Ecoindicator 99 (considered a precursor of the current ReCiPe 2016). The ReCiPe 2016 human health endpoint indicator (as well as Ecoindicator 99) addresses the damage to human health caused by respiratory and carcinogenic effects from organic and inorganic substances, human health issues caused by ionizing radiation, and climate change and ozone depletion. The ReCiPe 2016 ecosystem quality endpoint indicator (as well as Ecoindicator 99) addresses the damage to the ecosystem quality caused by ecotoxicological effects, land-use-related impacts, acidification and eutrophication.

Two frameworks also mentioned indicators at the endpoint level for climate change.[18,112] However, endpoint indicators for individual environmental aspects are much less commonly used in LCAs than midpoint indicators.

Some aspects are suggested at the conceptual level without suggesting a specific indicator and method in the reviewed frameworks. Ten frameworks remarked the importance of protecting biodiversity. In particular, the guides by BASF[54] and the US National Research Council[35] consider biodiversity conservation as one of the leading sustainability criteria. However, there is a lack of data or shared consensus on monitoring biodiversity losses *via* current LCA indicators.[35] Nonetheless, impacts on biodiversity are quantitatively strictly related to LCA endpoint indicators for damage to the ecosystem quality mentioned in the previous section.[113] Various (purely) conceptual frameworks have remarked the relevance of accounting for climate change issues, eco-toxicity, human toxicity, land use, and fossil/mineral resources.

The frameworks in the early stage of development showed a similar trend to the overall indicators adopted for the evaluation of the environmental dimension. This could be due to the fact that most of the indicators refer to midpoint impact categories of LCA. LCA can be performed also in the early stage as well as the estimation of the impact categories, being aware of higher uncertainty linked to the data availability and quality (see section 3.5 for further details). The slightly higher use of indicators on pressure was observed highlighting the higher availability of water and air emission information.

3.2.3 Social dimension. Table 4 shows the aspects and indicators mentioned by the reviewed frameworks under the social dimension. Aspects and indicators are clustered based on the potentially affected stakeholders, using the categories recommended in the UNEP.[32]

The 31 frameworks including the social dimension have often flagged aspects to be considered without proposing an indicator quantifying them based on a specific method. One of the reviewed studies remarked the lack of quantitative social assessments in common alternative assessment frameworks.[114]

As shown in Fig. 3, social impacts related to workers have the highest coverage in the revised framework, as 59% of total mentions of social aspects in the reviewed frameworks concerns the category "workers". The other stakeholder categories (local communities, value chain actors and society) have a lower coverage and the stakeholder category "children" (included in the last update of the UNEP Guidelines in 2020)

Table 4 Aspects and indicators related to stakeholders' categories with respective occurrence in the reviewed frameworks. Conceptual = just mentioned without recommending quantification based on a specific method or indicator

Stakeholder category Aspect/indicator	Number of frameworks adopted	Early stage application
Social	**189**	**20**
Consumer	**8**	**3**
Brand communication	1	1
Consumer acceptance	1	1
Consumer health & safety	1	
Content of natural substances (%)	2	1
Ethics in marketing communication	2	
Impact on basic needs of customers	1	
Local community	**41**	**5**
Access to basic needs	2	
Certified environmental management system	1	
Community acceptance	2	
Drinking water coverage	1	
Embodied forest area footprints	1	
Embodied agricultural area footprints	1	
Extraction of material resources	1	
Human rights (conceptual)	5	1
Human rights (LCA impact category)	2	
Human satisfaction (appropriateness for culture and level of noise and vibration)	2	1
Impact on the local economy	1	
International migrant stock	1	
International migrant workers in the sector	1	
Level of industrial water use	1	
Local employment	11	2
Net migration rate	1	
Pollution level of the country	1	
Public welfare and safety	2	
Respect to indigenous rights	1	
Respect to the living conditions	1	1
Sanitation coverage	1	
Unemployment rate	1	
Society	**17**	
Active involvement of enterprises in corruption and bribery	1	
Contribution to economic development	1	
Corruption prevention initiatives	4	
Health expenditure	1	
Illiteracy rate	1	
Life expectancy at birth	3	
Poverty alleviation	1	
Public expenditure on education	1	
Public sector corruption	1	
Risk of conflicts	1	
Value added	1	
Youth illiteracy	1	
Value chain actors	**13**	**4**
Fair competition	1	
Promoting social responsibility	2	1
Regional materials	2	1
Supply chain responsibility score	3	1
Tracking capacity	5	1
Workers	**110**	**8**
Accident rates at the workplace	1	
Age	2	
Annual job training	2	
Association and bargaining rights	1	
Child labour	12	2
Disability	2	
Equal opportunities and discrimination	9	
Evidence of violations of laws and employment regulations	1	
Fair salary	9	
Forced labour	11	1
Freedom of association and collective bargaining	7	1
Gender wage gap	1	
Labour influence	1	
Men in the sectoral labour force	1	
Noise reduction	4	
Part-time work	4	
Presence of sufficient safety measures	1	
Rate of injuries	3	
Respect to the national standards for security and social responsibility	6	1
Sexual harassment	4	
Social security and expenditure	1	
Time of exposure	1	
Trade unionism	1	
Trafficking in person	1	
Weekly hours of work per employee	1	
Women in the sectoral labour force	1	
Workers affected by natural disasters	1	
Workers' health & safety	11	3
Working conditions (LCA impact category)	1	
Working hours (*e.g.* maximum)/work–life balance	9	

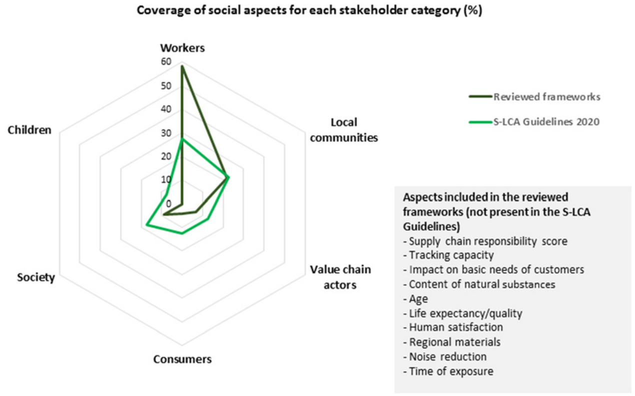

Fig. 3 Comparison of the coverage of social aspects in the reviewed frameworks and in the UNEP Guidelines on S-LCA[32], considering the various stakeholders' categories. In the case of S-LCA, shares refer to the total number of impact subcategories recommended in the UNEP Guidelines. For the reviewed frameworks, shares refer to the mentions of social aspects concerning the six stakeholder categories. A detailed list of aspects is available in the ESI.†

is not represented at all. The higher coverage of aspects related to workers can be explained by the higher data availability for work-related aspects, which usually are also easier to measure through quantitative indicators. Impacts on local communities, while being very relevant when assessing sustainability of product alternatives, are usually more difficult to assess due to the need for site-specific data. Impacts on society and value chain actors can also be challenging to assess given that in some cases the impact pathway is less defined. For what concerns impacts on consumers, they are to a large extent covered under the safety assessment.

Fig. 3 also lists additional social aspects found in the literature review that are not explicitly or completely addressed in the UNEP Guidelines.

The social aspects that are included in the highest number of frameworks are child labour,[12] forced labour,[11] workers health and safety[11] (in the stakeholder category "workers") and local employment[11] (under the stakeholder category "local community"). For the stakeholder category "value chain actors" the tracking capacity is included in 5 frameworks, while under the category "society" the aspect included the most is corruption prevention initiatives (4 frameworks), while the other two frameworks include other corruption-related aspects. For the "consumers" category the aspects ethics in marketing communication and content of natural substances are both included in two frameworks.

For what concerns positive impacts, which should capture the potential value for society or other stakeholders arising from a production and/or consumption activity, only the aspects local employment and contribution to economic development are included in the reviewed frameworks. While positive impact assessment is poorly implemented in practice (also due to the multiple conceptual definitions that can be adopted), there is clear interest in including this perspective in the sustainability assessment.[115]

Table 4 also shows that social dimension is seldom included in the sustainability assessment in the early stage of development. Among the indicators adopted in the early stage, worker-related aspects are the most assessed by few authors either from academia[53,116–118] and international organization.[119]

3.3.4 Economic dimension.

Table 5 shows the indicators under the economic dimension mentioned by the reviewed frameworks.

As shown in Table 5 indicators under the economic dimension are related to external cost, internal costs, profitability, value chain actors and others. The indicators related to internal costs are included in the highest number of frameworks[59] and in particular the total production cost is mentioned in 26 frameworks.

Profitability was remarked as a relevant concept in various frameworks. Four frameworks include financial profit as a quantitative indicator to measure it, while four frameworks proposed the indicator net present value. In 8 frameworks profitability was included without specifying a quantitative indicator to measure it.

The life cycle cost was recommended in 17 reviewed frameworks. In most of these frameworks, the life cycle cost calculation was combined with environmental LCA. Several frameworks, especially from scientific articles, mentioned accounting for the externality cost and the cost of waste generated. Potentially, methods for calculating life cycle costs could include externality costs caused by life cycle environmental impacts and land eco-remediation. Analogously, social LCA impacts such as worker safety and health protection could be included in life cycle cost methods.

As observed in a critical evaluation of economic approaches performed in the EU project Orienting,§§[120] a variety of Life Cycle Costing (LCC) methods have been proposed in the literature. The three main types of LCC include: conventional LCC, environmental LCC, and social LCC. This methodology, however, still lacks a general standard that provides guidelines for its use/application.[121]

Table 6 shows the economic indicators that have been detected in the frameworks revised in this study and their comparison with those reported in two reviews of sustainability assessment methodologies.[122,123]

The comparison shows that a variety of indicators can be applied, depending on the scope and the perspective of the economic analysis. The assessment of externalities is still poorly implemented, while profitability indicators are included in the three reviews under considerations, showing that, at this point, the methodology is mainly applied to assess company-related financial performance, rather than actual sustainability impacts.

The economic dimension is also addressed in frameworks regarding the early stage of development. In total, 34 frameworks include aspects, mostly on profitability and internal

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§§ Operational Life Cycle Sustainability Assessment Methodology Supporting Decisions Towards a Circular Economy, grant agreement no 958231.

Table 5 Indicators related to economic aspects with respective occurrence in the reviewed frameworks. Conceptual = just mentioned without recommending quantification based on a specific method or indicator

Aspect Indicator	Number of frameworks adopted	Early stage application
Economic	**143**	**63**
External cost	**24**	**4**
Externality cost [€]	3	
Life cycle cost [€]	17	3
Waste (incl. emissions)/recycling treatment cost	4	1
Internal cost	59	27
(Total) production cost [€]	26	15
Cost of maintenance/repairs	3	1
Product cost	6	1
Purchase cost	20	7
SSbD implementation costs	1	1
Total Annual Cost (TAC)	3	2
Profitability	**25**	**14**
Added value [€]	1	
Financial profit [€]	4	2
Minimum selling price [€]	4	2
Net present value [€]	4	4
Normalised added value [-]	1	
Payback period [years]	1	1
Profitability (conceptual)	8	3
Total capital investment	1	1
Yield	1	1
Value chain actors	**5**	
Product performance	1	
Stakeholder requirements	1	
Transparency and information	1	
Value chain collaboration	1	
Willingness to pay	1	
Other	**38**	**23**
Additional income (incentives, flexibility, and additional area)	1	
Affordability	1	
Breakeven point	1	1
Comfort of occupants	1	
Customer acceptance and satisfaction	1	
Discounted cash flow rate of return	1	1
Feedstock price	2	2
Flash point	1	1
Initial and maintenance budget	1	
Innovation potential (by number of publications)	1	1
Market acceptance	2	
Non-construction cost (tax, financial cost)	4	1
Performance uncertainty (material never used in a context)	1	1
Point of explosion	1	1
Predictability	1	
Process cost	2	2
Projected price	1	1
Reaction and resistance to fire	1	1
Scalability	1	
Waste management cost	7	6
Total Capital Cost (TCC)	3	2
Total Production Cost (TPC)	3	2

costs, mostly by academia. Smith *et al.* are the only ones from an international agency introducing the GREENSCOPE indicators for the design including also indicators for the economic dimension.[81]

3.3 Life cycle thinking considerations

About 60% of the selected frameworks consider LCA a key method to assess sustainability aspects. The idea to integrate the life cycle environmental impacts with risk assessment has a long history in solvent selection frameworks which started in the early nineties.[75,76,124] For example, compared to the risk assessment used to cover safety aspects, the LCA methodology can broaden the scope to include climate change impacts.[125] The two methods could potentially be used either combined or in parallel.[126,127]

The frameworks reviewed often pointed out that a cradle-to-grave comparison of the final application (product or service) is necessary to evaluate chemicals' safety and sustainability compared to the alternatives. However, the reviewed frameworks rarely provided clear recommendations on when a cradle-to-gate comparison of chemicals is considered enough and when a cradle-to-grave LCA evaluation becomes necessary.

To optimize the time needed to conduct an LCA, several scientific articles[77,126,128,129] presented various easy-to-use LCA-based tools allowing preliminary environmental profiling, especially for the early stage of development. Examples of them include: (i) the FLASC tool calculates preliminary cradle-to-gate impacts for eight impact categories for a wide range of materials commonly used in drug manufacture;[77] (ii) the Q-SA$\sqrt{}$ESS (Quick Sustainability Assessment *via* Experimental Solvent Selection) methodology calculates six cradle-to-grave sustainability metrics for the three "most sustainable solvents" for a specific process;[130] and, (iii) the US EPA (United States Environmental Protection Agency) created a method rapidly generating life cycle inventories from publicly available databases by allocating the emissions from facilities related to the production of the chemical of interest.[131]

Other leading streamlined LCA tools are the ecosolvent tool[132] for solvents, the LICARA NanoSCAN tool[133] for nanomaterials and other models proposed by recent literature for application to a broad range of chemicals (*e.g.* ref. 126). Tools for streamlined LCAs can provide valuable decision support for chemicals in their early stage of development when data availability is very limited. However, the results generated using such tools have high uncertainty especially due to low technological, geographical and temporal representativeness. Hence, robust evaluations can be generated only *via* full LCAs.

Alternatively, previous studies[128,134] proposed the use of physicochemical properties to predict the life cycle environmental impact in the early stage of development. Their approach assumes that there is a link between those properties and the environmental performance of the chemical production process being developed and assessed. Finally, Pizzol *et al.*[135] recently proposed and tested a tiered approach with qualitative assessment for safety, environmental, and social dimensions in the early stage of development.

While several environmental LCAs of nanotechnologies have already been published,[136,137] various studies acknowledged the challenges of conducting LCAs of nanomaterials due to their complexity and dynamic behavior during the life

Table 6 Comparison between the economic indicators reported in the revised frameworks for SSbD chemicals and the literature reviews published in Alejandrino *et al.* (2021)[122] and Visentin *et al.* (2020)[123]

	Economic indicator	Alejandrino *et al.* 2021[122]	Visentin *et al.* 2020[123]	Revised frameworks
External cost	Externality cost		✓	✓
	Life cycle cost		✓	✓
	Waste (incl. emissions)/recycling treatment cost			✓
Internal cost	(Total) production cost	✓	✓	✓
	Cost of maintenance/repairs		✓	✓
	Product cost			✓
	Purchase cost			✓
	SSbD implementation costs			✓
	Total Annual Cost (TAC)			✓
	Electricity cost		✓	
	Cost of capital		✓	
	Raw material cost			
	Labour cost		✓	
Profitability	Added value	✓		✓
	Financial profit	✓		✓
	Minimum selling price			✓
	Net present value	✓	✓	✓
	Normalised added value			✓
	Payback period	✓		✓
	Profitability		✓	✓
	Total capital investment	✓		✓
	Yield			✓
	Internal rate return	✓		
	Revenues			
Value chain actors	Product performance			✓
	Stakeholder requirements			✓
	Transparency and information			✓
	Value chain collaboration			✓
	Willingness to pay			✓
Other	Additional income (incentives, flexibility, and additional area)		✓	
	Affordability			✓
	Breakeven point			✓
	Comfort of occupants			✓
	Customer acceptance and satisfaction			✓
	Discounted cash flow rate of return			✓
	Feedstock price			✓
	Flash point			✓
	Initial and maintenance budget			✓
	Innovation potential (by number of publications)			✓
	Market acceptance			✓
	Non-construction cost (tax, financial cost)			✓
	Performance uncertainty (material never used in a context)		✓	
	Point of explosion			✓
	Predictability			✓
	Price	✓		
	Process cost			✓
	Projected price			✓
	Reaction and resistance to fire			✓
	Scalability			✓
	Waste management cost			✓
	Total Capital Cost (TCC)			✓
	Total Production Cost (TPC)			✓
	Economic impact score	✓		
	Financial incentives	✓		
	Risk	✓		
	GDP/contribution to GDP	✓		
	Investment	✓		

cycle.[138–140] However, an effort is currently ongoing to fill this gap. Such an effort is ongoing also for LCAs covering social and economic aspects.[141] In particular, LCA guidelines for manufactured nanomaterials were released in 2018.[142]

The environmental assessment of chemicals has been evolving and moving from typical green chemistry mass-based metrics to a life-cycle perspective, as this was identified as indispensable to verify actual environmental benefits.[17,130,143]

3.4 Decision-making support: evaluation and trade-offs

Rarely, a certain chemical is optimal for all safety and sustainability aspects *e.g.* it might not present hazard concerns but require a high amount of energy for its production, resulting, for example, in high climate change impacts. Therefore, the assessment of safety and sustainability of chemicals should include a procedure to support decision making considering as well existing trade-offs.[144]

The preliminary step in frameworks assessing safety and sustainability of alternative chemicals is the identification of alternatives and its technical performance. The technical performance in fulfilling the function of the candidate alternative and of the alternatives in providing such functions is established *via* techno-feasibility assessments.[18,35,144,145] New or alternative chemicals should be compared based on equal functional performances using "substitution factors" and for LCA using a "functional unit". Nevertheless, a calculation procedure for substitution factors for a specific function and/or a structured method to detect respective alternatives was rarely reported.

Then, the safety performance of the alternatives scrutinizing physicochemical properties and applying risk assessment is evaluated. If safety is part of the framework, the evaluation of environmental, social, and economic aspects is conducted only for chemicals passing the safety assessment.

In the case of social impact assessment, compensation between positive and negative impacts should be avoided. Moreover, when assessing positive impacts, great caution must be taken with the inclusion of product utilities and when comparing the positives for one stakeholder group with the negatives for another. Indeed, as observed by Croes *et al.*[146] an imprudent inclusion of positive impacts might led to white-washing practices and loss of credibility of the assessment.

The vast majority of frameworks provide a separate outcome for each aspect considered or at least per dimension (safety, environmental, social, and economic). For example, a chemical can have the outcome "recommended" in the environmental dimension but "problematic" in the safety dimension or *vice versa*.[62] The decision is then left to the user of the outcome, leaving an appropriate degree of freedom on the final decision. In particular, if safety is part of the assessment, an aggregated score over multiple sustainability dimensions is not recommended to avoid compensation between different impacts. To facilitate decision making, the impact profiles of the alternatives can also be presented at the highest aggregated level with single scores per dimension.[18,62]

The score is often translated in colour coding based on a percentage performance indicator, *e.g.* 0% representing the no sustainability (the alternative performs the worst in that aspect) and 100% representing the highest sustainability (the alternative performs the best in that aspect), and this is particularly the case of frameworks developed for the early stage.[81] Pfizer was one of the first companies to use color-coding to categorize solvents (green = preferred, amber = usable and red = undesirable).[147] A similar coding system has also been proposed by other companies *e.g.* Sanofi, Astra Zeneca and GSK[77,148,149] and environmental agencies *e.g.* the German Environment Agency.[150]

In most cases, color-coding is applied to the outcome of each criterion to evaluate safety, health, and environmental aspects.[73,148,150] For example, each chemical can get a score between 1 and 10 for each criterion, which is then translated into the 3-color code (*e.g.* green, yellow, and red).[62,73,130,148,149,151] Except for green, the meaning of the other colours can be slightly different, *e.g.* red can mean undesirable[147] or substitution requested.[148,150] Some guides use brown to catalogue banned chemicals (*e.g.* ref. 148). White colour is often used for data unavailability that does not allow the assessment for a certain criterion.[148–150] Sometimes also orange is included as a colour to indicate a chemical that should be substituted but does not have to if it is still compliant with current regulation.[73]

Other approaches to support decision making suggested in the literature include the use of Multi-Objective Optimization (MOO) techniques or Multi-Criteria Decision Analysis (MCDA). MOO frameworks for alternative assessment are normally implemented in computer-aided molecular design tools using for example a Fuzzy Analytic Hierarchy Process (FAHP) weighting approach.[63,152] This means that the decision-making is structured as a hierarchy where the primary goal of the design *e.g.* safety comes before other criteria and sub-criteria, giving priority to the objects of the decision problem that must be fulfilled.[63,152] Regarding the design, simple hotspot analysis is also conducted to guide further development of the design of the new chemical or material.[153]

MCDA, which allows simultaneous comparison of multiple and often conflicting aspects, has also been highlighted as a key instrument for sustainability assessment, as discussed in major works and reviews.[29,30,154] Two commonly used MCDA methods are the multi-attribute utility theory and outranking.[61] Although MCDA methods may be useful in providing decision makers with a common baseline to understand the performance of alternatives and the trade-offs they present, they may be significantly resource intensive. MCDA in the early stage of development have been found to be recently explored by few authors. Garas *et al.*[117] adopted a Sustainable Decision Support System (SDSS) scoring system that integrates LCA and MCDA; García-Velásquez C.[155] used the Pareto frontiers to guide decision in the plastic sector. Finally, Manjunatheshwara and Vinodh adopted a grey method for the decision specifically for materials selection at the design phase with uncertain conditions.[156]

3.5 Data availability and uncertainty

A key issue in sustainability assessment of chemicals and, in particular, of new ones, is the lack of data and data uncertainty.

Some of the frameworks propose ways to deal with data gaps, reflecting this in the evaluation. Malloy *et al.*[61] applied an MCDA framework to assess the impact of data gaps on alternative assessment using multi-attribute utility theory and outranking other tools, penalising aspects with missing data by applying a lower score (GreenScreen full assessment, SciVera, GreenSuite); other tools, usually list-based tools, consider missing data as undetermined (GreenScreen List Translator) or indifferent on the final score (GreenWERCS).[157]

GreenSuite's procedure uses five criteria to differentiate the cause of the missing data to score the aspect as more hazardous.[158]

The GreenScreen® tool (and by extension, the IC2[159] and Rossi[44] frameworks) propose a system based on the preliminary score to assess the level of the material analysed, in which data gap analysis is applied to determine if the data requirements are met. If the analysis fails, the final score is lowered by one unit, otherwise the score is confirmed.[45]

OECD[160] addresses data gaps by using two different approaches, depending on whether the data quality is limited (tier 1) or whether high quality data are used (tier 2), stating the quality of the assessment to the audience.

Regarding uncertainty assessment, a limited number of frameworks have suggested ways to perform it. NRC[157] suggests a list of good practices to deal with uncertainties that include the selection of alternatives with only known aspects and conducting a quantitative analysis, pointing out that when uncertainty is large enough to overwhelm any relative differences between alternatives, it becomes impossible to determine any better alternative. Safe Consumer Products[161] provide a stepwise approach to carry-out uncertainty assessment and data gaps.

Although the assessment of chemicals or materials in the early stage of development is quite uncertain due to the lack or quality of data, only 9 authors focused on sensitivity analyses or uncertainty, most of them regarding construction and solvent sectors. Among available options, Posada *et al.* performed a Monte Carlo simulation to identify the variability on the input data, and similarly, Zapata Boada *et al.* analysed the influence of parameters affecting economic and environmental performances by sensitivity analysis. In addition, the Triangular Fuzzy Number and Fuzzy Topsis,[152,162] the VEGA toolbox[163] and the IDEMAT 2001 database[164] have been used to evaluate variability and uncertainty. Uncertainty assessment is key for early stage assessments as it provides the decision maker the spectrum of possibilities enabling a more informed decision making. At a minimum, sensitivity analysis should be conducted on key parameters in the system to study the robustness of results and their sensitivity to uncertainty factors. This will determine whether data collection and quality need to be improved and enhance the interpretation of results.

4. Conclusion

This review focused on how sustainability has been implemented in frameworks used to assess the safety and sustainability of chemicals and materials. In particular, frameworks integrating more than one sustainability dimension among safety, environmental, social, and economic were analysed and to which extent they were applied in the early stages of development of chemicals and materials.

While some of the reviewed frameworks are conceptual, other frameworks provide a detailed guideline to support the selection of safer and more sustainable chemicals. Most reviewed frameworks pointed out that the criteria regarding safety and sustainability of alternatives should be based on equal functional performance. However, they lack providing a calculation procedure of substitution factors for a specific function and a structured method to detect respective alternatives.

A major focus was on scrutinizing sustainability aspects and indicators and respective calculation methods as well as the decision procedures proposed by the frameworks. The intent was to understand the current state of art and gaps to reach a better-informed decision-making process for designing or selecting safe and sustainable chemicals. This review highlighted that there is no uniform and comprehensive set of indicators for examining the sustainability of a chemical within proposals of frameworks from academia, governments, NGOs, or industry, especially for what concerns socio-economic aspects. This fact could negatively impact the roadmaps of chemicals since they might be sustainable according to one framework but not another.

In this sense, LCA can be of use as it covers multiple environmental impacts. In fact, there was a broad consensus on the need to account for the life cycle of chemicals and on the need to use indicators based on the life cycle assessment methodology. In fact, LCA can overcome the limitation of simple mass- and energy-based metrics that do not capture actual shifts in environmental burdens by selecting an alternative instead of another. LCA has been gaining prominence in sustainability assessment nonetheless there are limitations that need to be addressed to ensure robust assessments. In particular, guidance is needed for LCA modelling of technologies at a low technology readiness level and for which the data gaps and uncertainty are even more predominant. While the S-LCA does not have the same level of maturity as the environmental LCA, this methodology underpins internationally agreed guidelines that can be taken as a reference, especially for what concerns the list of social aspects to be selected for the assessment, and as general guidance for the social assessment. The LCC methodology is the most heterogeneous for what concerns the methodological approach but also from a conceptual point of view (which kind of impacts should be assessed, area to be protected, *etc.*).

Increasing chemicals' circularity is also acknowledged by the EU CSS as a way to contribute to reducing chemical pollution in wastewaters. However, mass-based/circularity metrics in the reviewed frameworks do not account for the effect of multiple cycles in environmental assessment as well as hazard and risk assessments. Therefore, as also remarked by the EU CSS, there is a need to develop methodologies for chemical risk assessment that take into account the whole life cycle and the effect of increased circularity.

To have the "paradigm shift" towards safe and sustainable chemicals, the industry and sustainability/LCA community need to respond to the challenges resulting from this review. Numerous organizations already have many initiatives, but these are carried out mainly independently. With a lack of coordination, it is difficult to guarantee a harmonized selection of suitable sustainability indicators to be integrated into future frameworks. This review shows that there is no uniform set of indicators within proposals of frameworks from academia, governments, NGOs, or industry for evaluating the sustainability of chemicals. If different indicators are implemented in the various frameworks developed in parallel for the same context, they can negatively impact the product roadmaps that often take years for development.

Author contributions

Carla Caldeira: conceptualization, methodology, investigation, visualization, and writing – original draft; Elisabetta Abbate: investigation, visualization, and writing – review & editing; Christian Moretti: investigation, methodology, and writing – original draft; Lucia Mancini: investigation, methodology, and writing – review & editing; Serenella Sala: conceptualization, writing – review & editing, and supervision.

Conflicts of interest

There are no conflicts to declare.

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