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Screening level approach to support companies in making safe and sustainable by design decisions at the early stages of innovation

Lisa Pizzol[a], Arianna Livieri[a,b], Beatrice Salieri[c], Lucian Farcal[d], Lya G. Soeteman-Hernández[e], Hubert Rauscher[d], Alex Zabeo[a], Magda Blosi[f], Anna Luisa Costa[f], Willie Peijnenburg[e,g], Stella Stoycheva[h,l], Neil Hunt[h], Maria José López-Tendero[i], Cástor Salgado[j], Julian J. Reinosa[j], Jose F. Fernández[k], Danail Hristozov[l,*]

[a] GreenDecision srl, Via Torino 155, 30172, Mestre, Venezia, VE, Italy
[b] Department of Environmental Sciences, Informatics and Statistics, Ca' Foscari University of Venice, Venice, Italy
[c] TEMAS Solutions GmbH, Lätteweg 5, 5212, Hausen, Switzerland
[d] European Commission, Joint Research Centre (JRC), Ispra, Italy
[e] National Institute for Public Health and the Environment (RIVM), Center for Safety of Substances and Products, Bilthoven, the Netherlands
[f] National Research Council of Italy-Institute of Science, Technology and Sustainability for Ceramics, CNR - ISSMC (former ISTEC), Faenza, Italy
[g] Institute of Environmental Sciences (CML), Leiden University, P. O. Box 9518, 2300, RA, Leiden, the Netherlands
[h] Yordas Group, Äußere Nürnberger Straße 62, 91301, Forchheim, Germany
[i] Laurentia Technologies SLL, Benjamin Franklin 12, 46980, Paterna, Valencia, Spain
[j] Encapsulae SL, Lituania 10, 12006, Castellón de la Plana, Spain
[k] Instituto de Ceramica y Vidrio, CSIC, Kelsen 5, 28049, Madrid, Spain
[l] East European Research and Innovation Enterprise (EMERGE), Otets Paisiy 46, 1303, Sofia, Bulgaria

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ABSTRACT

The European Green Deal policy ambitions set out in the Chemicals Strategy for Sustainability and the Zero Pollution Action Plan identify the transition to a Safe and Sustainable by Design (SSbD) approach to chemicals and materials. The H2020 SUNSHINE project has developed an approach to operationalize SSbD, specifically addressing multi-component nanomaterials (MCNMs), and applied it to two case studies. This approach enables assessment of safety and sustainability aspects at each stage of product development from a lifecycle perspective. This is achieved via a tiered approach that uses qualitative (Tier 1), semi-quantitative (Tier 2) and quantitative (Tier 3) assessment methods. The present work focuses on the Tier 1 (self-assessment) methodology designed to evaluate the safety, functionality and sustainability in the early R&D stages of the lifecycle of chemicals and materials. This approach was developed to be implementable by industries in a straightforward manner as often there is lack of time and/or expertise to engage in resource-intensive safety and sustainability evaluations. The approach was tested using two real industrial case studies, namely nano-enabled PFAS (Polyfluoroalkyl substances)-free anti-sticking coating for bakery molds, and nano-drops of essential oil anchored to the surface of nano clays and encapsulated in a polymeric film. The results indicate that these innovative materials have a high probability to have better safety, functionality and sustainability performance compared to conventional benchmark materials.

1. Introduction

The European Green Deal aims at transforming the EU's economy to a more sustainable one with policies addressing climate, biodiversity, circularity, human health and environmental protection (European Commission, 2019). This includes an ambitious plan to tackle pollution from all sources and progress towards a zero-pollution economy for a toxic-free environment. The Chemicals Strategy for Sustainability (CSS) and the Zero Pollution Action Plan are driven by the Green Deal ambitions, identify actions to reach them and call for a transition towards a Safe and Sustainable by Design (SSbD) approach for chemicals and emerging advanced materials (European Commission, 2021) (European

* Corresponding author.
E-mail address: danail.hristozov@emerge.bg (D. Hristozov).

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Commission, 2020). In response to this, the European Commission (EC) published the Recommendation for establishing a European assessment framework for 'safe and sustainable by design' chemicals and materials (European Commission, 2022), which is based on a holistic scientific-technical approach developed by the EC's Joint Research Centre (C. Caldeira et al., 2022). In the following sections, the EC Recommendation (European Commission, 2022) in combination with its scientific-technical background (C. Caldeira et al., 2022) will be called the "SSbD Framework". The SSbD Framework highlights that assessing health, environmental, social, and economic impacts requires integrated approaches to be able to address complex systems and to enable reproducible and transparent comparison of alternatives to select safer and more sustainable design options (C. Caldeira et al., 2022). According to the EC Recommendation (European Commission, 2022), the proposed framework is based on a tiered approach depending on data availability, considering that the information available for newly developed chemicals or materials could be limited at the beginning of the process, while it increases along the product development process. Methods and standards are available to assess safety and sustainability during the later phases of the product development. However, simplified methods which can be applied in the early stage of product development are still lacking or in the initial stage of development. Specifically, in the initial product R&D phases, where quantitative information on the material/product manufacturing, use and end of life can be patchy or even missing, there is a need for qualitative, screening approaches which are able to identify potential safety and sustainability issues at an early R&D phase. Screening approaches can also reveal information gaps and raise awareness of potential safety and sustainability concerns, which may in turn trigger the need for regulatory action.

Several frameworks exist that aim to combine safety and environmental, economic, and social assessments from a sustainable development perspective. Examples of frameworks primarily focusing on chemicals and not specifically addressing nanomaterials and MCNMs include the work developed by the company Evonik (2020), by the Interstate Chemicals Clearinghouse (IC2, 2017), by the Alternatives Assessment Framework proposed by Rossi and colleagues (Rossi et al., 2006), by the UB (Umweltbundesamt (Hrsg.), 2016), and by WBCSD (World Business Council for Sustainable Development) (WBCSDwbcsd, 2018). Additionally, there are some frameworks that do focus on nanomaterials, such as the LICARA nanoscan (Van Harmelen et al., 2016), which covers public health and environmental risks, occupational and consumer health risks, but also environmental, economic and societal benefits. Nevertheless, LICARA nanoscan is semi-quantitative and does not consider the functionality aspect that the proposed approach does. The proposed approach evaluates all aspects of safety and sustainability for all life cycle stages (raw material acquisition, production of the MCNM, production for the product incorporating the MCNM, use, and end-of-life), whereas LICARA nanoscan only focuses on specific stages (production, use, and end-of-life). Additionally, the "Precautionary Matrix" (Höck et al., 2010) is a useful tool for identifying possible risks in the development, production, use, and disposal of synthetic nanomaterials. However, it places less emphasis on sustainability. On the other hand, ReCiPe (Goedkoop et al., 2009) specifically addresses sustainability aspects, but primarily in a quantitative manner.

As far as the definition of SSbD is concerned, the CSS describes it as: "a pre-market approach to chemicals design that focuses on providing a function (or service), while avoiding volumes and chemical properties that may be harmful to human health or the environment, in particular groups of chemicals likely to be (eco) toxic, persistent, bio-accumulative, or mobile. In this context, the overall sustainability should be ensured by minimising the environmental footprint of chemicals in particular on climate change, resource use, ecosystems and biodiversity from a life cycle perspective" (European Commission, 2020). Also, "the SSbD approach addresses the safety and sustainability of the material/chemical/product and associated processes along the whole life cycle, including all the steps of the research and development (R&D) phase, production, use, recycling and disposal" (OECD, 2022).

Some categories of multi-component nanomaterials (MCNMs) can be considered Advanced Materials according to the OECD's description of the term (OECD, 2023). These materials are often referred to as being among those Key Enabling Technologies (KETs) that could support the transition towards more sustainable innovation in key industrial sectors such as construction, structural and functional materials, active ingredients, food, healthcare, energy, cosmetics and electronics (Gottardo et al., 2021) (Samani et al., 2015; Zheng et al., 2021). The term MCNM itself is not yet well established, neither in a scientific nor in a regulatory context. MCNM may be described as materials that consist of two or more functional components (e.g., nanoparticles, organic molecules, etc.) conjugated by strong molecular bonds, or formed by a nanomaterial (NM) with a unique chemical origin modified by hard or soft coatings (Banin et al., 2014); (Saleh et al., 2015). Some of the most widely used components are (combinations of) carbonaceous (e.g., fullerenes, carbon nanotubes, graphene) or metallic (metal or metal oxide) NMs with or without organic coatings (e.g., polymers, macromolecules and enzymes).

MCNMs can offer significant technological benefits as the integration of different components in a unique system can produce new or improved functionalities. However, MCNMs can also pose substantial design challenges as well as environmental, health and safety (EHS) concerns (Furxhi et al., 2022). The latter are particularly complex due to the differing rates of degradation and different toxicity of the separate and interacting components, and their more complex interactions with biological and environmental systems (Banin et al., 2014; Huang et al., 2018; Saleh et al., 2015). These concerns have raised questions regarding not only the EHS implications of these materials, but also their overall sustainability (Mech et al., 2022).

The European H2020 SUNSHINE project (h2020sunshine.eu) strives to provide answers to some of these questions. Its goal is to develop an overarching approach for SSbD of MCNMs and demonstrate it in industrially relevant case studies.

The developed SSbD approach supports industries with the modification and subsequent assessment of advanced materials/products in order to increase their safety and sustainability without compromising their functionality or commercial viability. The approach is comparative: i.e., the assessed SSbD-modified material is always compared to a benchmark. Such a benchmark could be for example an alternative design option or a conventional material/product that has the same or a similar function. The proposed SSbD approach follows the *Agile Stage-Gate Idea-to-Launch* innovation model (Cooper, 2014; Cooper and Sommer, 2018), which divides the innovation process into five Stages and requires analysis at each Gate to inform 'Go/No Go' decisions. In this way the *Agile Stage-Gate* approach continuously challenges the early stages of innovation to cost-efficiently develop safer, functional and more sustainable products. To develop the SSbD strategies and to prove that they are effective, a tiered approach is proposed. This approach uses screening-level qualitative (Tier 1) and semi-quantitative (Tier 2) methods to assess safety, functionality and sustainability at the early stages of product development (i.e. G2-G5), and quantitative (Tier 3) assessment methods for the later stages (i.e. G3 till Post-launch). The developed tiered approach assesses safety, functionality, and sustainability aspects in alignment with the framework for the definition of SSbD criteria and evaluation procedure for chemicals and advanced materials of the European Commission's Joint Research Centre (C. Caldeira et al., 2022).

In this context, 'safety' is seen as 'transversal to all sustainability dimensions (environmental, social and economic)' (C. Caldeira et al., 2022), and hence is an integral part of sustainability. In that quality, safety is specifically highlighted in the SSbD Framework. For example, certain environmental and human health safety related aspects (i.e., toxicity and exposure) can be used to assess also environmental sustainability and similarly, by addressing workplace safety, some social aspects of sustainability (e. g., child labor and local employment) can be

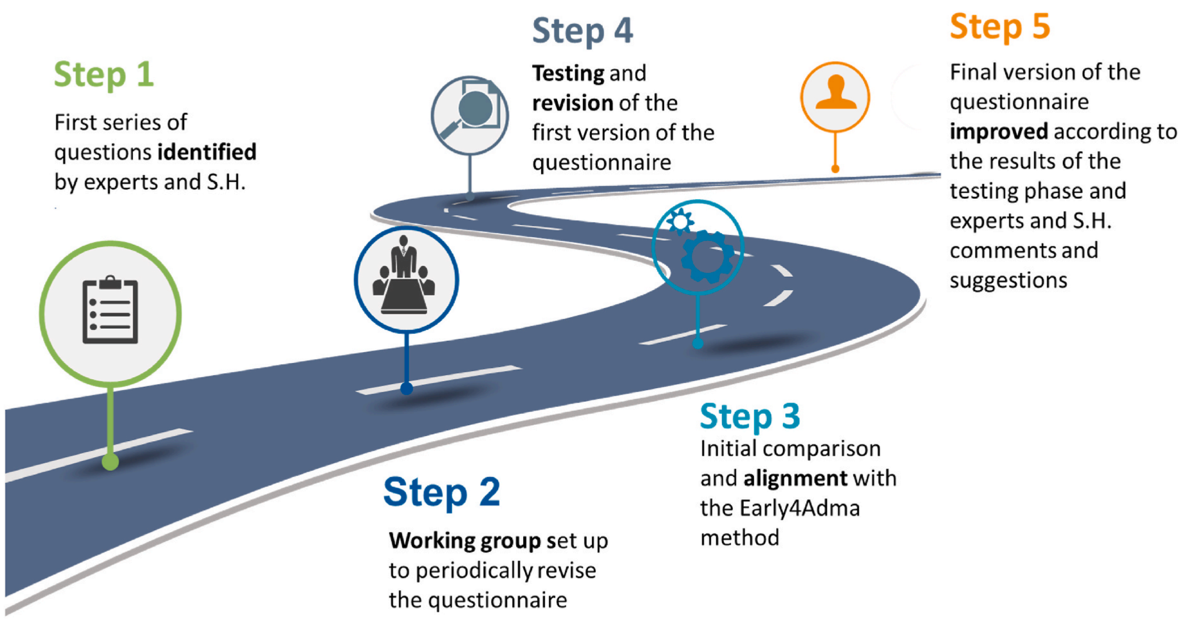

Fig. 1. Methodological steps to develop the questionnaire.

addressed too. The selected aspects cover the three main dimensions of sustainability and are aligned and contribute towards the achievement of most of the 17 Sustainable Development Goals, with the exception of SDG 1 - No poverty, SDG 2 - No hunger, SDG 4 - Quality education and SDG 16 - Peace, justice and strong institutions.

Finally, 'Functionality' is defined as the ability of a product to be useful and to achieve the goal for which it was designed. Criteria such as durability, performance, and reliability have been used to measure functionality (Tavernaro et al., 2021). Therefore, the case studies support the practical operationalization of the SSbD Framework to MCNMs.

The focus of this manuscript is particularly on the description of the qualitative Tier 1 self-assessment methodology to compare design alternatives that is composed of a questionnaire for pre-evaluation of safety, sustainability and functionality.

This methodology is then thoroughly illustrated in two case studies: the first consist of a novel PFAS-free anti-sticking coating used in the bakery industry (i.e., coating of baking trays and pans) compared to a conventional material (Teflon), and the second of nanodrops of essential oil anchored at the surface of nanoclays and encapsulated in a polymeric film compared to a conventional food packaging (LDPE) for food packaging which keep the packaged food free of insect pests. The process for the development of the Tier 1 methodology is described in the methods section, along with the description of the two case studies where the developed methodology has been applied. The results section provides a detailed explanation of the developed tiered approach's structure, the description of the Tier 1 questionnaire, including its division into four parts, the answers collected for the two case studies and their assessment. These results are then discussed in the fourth section, while the conclusions are reported in the fifth section.

2. Methods

Following the adoption of the EC's SSbD Framework, the SUNSHINE experts have developed a tiered approach to operationalize it. The reason for adopting different tiers for the assessment stems from considerations that the information available for newly developed chemicals or materials could be limited in the early stages of development (e.g., R&D stage), while availability of data and expertise increases in the later product development and optimization stages, which also demand more thorough assessment of safety and sustainability. However, the early R&D stage of chemicals or materials development plays a central role in the innovation process while few low-tier assessment methodologies are available to address it. This is why in this manuscript we strive to address this gap by developing a self-assessment methodology for SSbD able to compare design alternatives by means of a questionnaire for pre-evaluation of safety, sustainability and functionality.

As reported in Fig. 1, to reach this objective, a first series of questions were identified in co-creation with key stakeholders (S.H.) from industry, regulation, policy, academia, all inspired by "Safe and Sustainable by Design chemicals and materials: Framework for the definition of criteria and evaluation procedure for chemicals and materials" (Step 1) (C. Caldeira et al., 2022). Specifically, a working group of experts in developing frameworks for SbD and risk assessment of NMs from EU projects along with experts in environmental and socio-economic sustainability was set up, which periodically met to frame the questionnaire and identify the relevant questions (Step 2).

These questions were targeted at innovators from industry, especially SMEs, and were aligned with the questions of "Towards Safe and Sustainable Advanced (Nano)materials: A proposal for an early awareness and action system for advanced materials (Early4AdMa)" (Step 3) (Oomen et al., 2022), which in contrast targets regulators and policy makers. The scope of the questions of the proposed self-assessment methodology addresses the safety, functionality, and sustainability of advanced materials, with a special focus on socioeconomic aspects. On that basis, a first version of a questionnaire was released and tested in the case studies of the SUNSHINE project (Step 4). The results were further discussed and elaborated, so that the questions related to the safety and functionality aspects were improved thanks to a stronger collaboration with industries and experts in regulatory risk assessment. The questions pertaining to socioeconomic aspects were improved though the alignment with the categories and subcategories provided by previously developed approaches such as (Stoycheva et al., 2022) and the UNEP methodological sheets (Step 5) (UNEP, 2021).

In the final version of the questionnaire, the experts decided which questions were relevant for screening of safety, sustainability, and functionality along five life cycle stages (LCS): i.e., (1) Raw materials and resources needed to produce the material/product, (2) Production of the MCNM, (3) Production of the product incorporating the MCNM, (4) Use of the product, and (5) End of Life treatment.

Regarding the **safety dimension**, the eventual presence of hazardous materials, such as carcinogenic, genotoxic, endocrine disrupting, and the physical hazard properties of the MCNM were investigated along

Table 1
Possible components of the $SiC@TiO_2$

MATERIAL	COMPONENTS	Nomenclature
Core-shell SiC–TiO2 (silicon carbide - titanium dioxide)	**$SiC–TiO_2$ 60 nm**	1.1_SiC@TiO2_60
	$SiC–TiO_2$ 500 nm	1.1_SiC@TiO2_500
	SiC 60 nm NPs	2.1_SiC_60
	SiC 500 nm NPs	2.1_SiC_500
	TiO2 shell material	3.1_TiO2

the LCS. At the same time, the release and emission of hazardous substances due to the production of the MCNM and the related enabled product, as e.g. the possible release of carcinogenic, persistent, bioaccumulating substances from the product, and the transformations of any released MCNM were also assessed along the LCS.

Regarding the **environmental sustainability dimension**, the use of critical and/or renewable materials, the energy sources, the use of water, as well as consideration related to generation of waste and greenhouse gas (GHG) emissions, chemical emissions in environmental compartments, possibility to recycle the waste generated during the production process and reusing any by-products/co-products were investigated.

For the **social sustainability dimension**, the following aspects were addressed: respect of the living conditions of affected local communities, the policies and restrictive procedures for the traceability of raw materials, minimization of social issues related to the acquisition of raw materials and resources, the promotion of regional products, the social responsibility of suppliers, the technological development and educational opportunities, and the screening of possible End of Life treatment options.

Regarding the **economic sustainability dimension**, the provision of the costs of the raw materials and their transport, the materials production, products manufacturing and waste disposal, the installation costs for implementing SSbD actions, the direct economic benefits in using the innovative product and the direct costs of the End-of-Life treatment were considered.

Finally, for the **functionality dimension**, characteristics such as durability, reliability, useability, versatility were investigated in the Use LCS.

The final version of the questionnaire (reported in the results section) was applied to two real industrial case studies.

2.1. *Description of the case studies*

2.1.1. *Laurentia Technologies*

Laurentia Technologies develops, produces and markets micro-encapsulated active ingredients and functional coatings based on nanomaterials. The material provided by the company and assessed for this case study is a nanocomposite coating composed of silica carbide and titanium dioxide ($SiC@TiO_2$) which provides non-stick properties on its applications in bread baking trays. This innovative material is a substitute for Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS)-based non-stick coatings, such as Teflon (Polytetrafluoroethylene or PTFE). Indeed, it is well known that exposure to high levels of some PFAS may cause adverse health effect including reduced antibody responses to vaccines, increased cholesterol levels, low infant birth weight, and increased risk of high blood pressure (Vorst et al., 2021). Therefore, industries are currently searching for ways to substitute Teflon-based coatings for safer and more sustainable alternatives.

Avoiding the use of toxic and carcinogenic substances such as PFAS is already a step forward towards safer products and it has been realised using Sol-Gel-Derived Silicon-Containing Hybrids modified with $SiC@TiO_2$ which enhances anti-sticking properties when applied as cover on baking trays. The presence of SiC in the core of the MCNM increases the mechanical and thermal properties, the durability, and enhances anti-sticking properties of the surface on which it is placed. Overall, two material components are used to produce the MCNM, a 60 nm $SiC@TiO_2$ and a 500 nm $SiC–TiO_2$. In Table 1 the possible components of the $SiC@TiO_2$ MCNM are summarised.

The considered benchmark is Polytetrafluoroethylene (PTFE) or Teflon, a resin used in many industries, thanks to its chemical, thermal and electrical stability and low friction (Sajid and Ilyas, 2017). Teflon is used as coating material in non-stick cookware to prevents food from sticking during the cooking process. At normal cooking temperatures, PTFE-coated releases chemicals and various gases exhibiting mild to severe toxicity. Moreover, the well-known toxic environmental pollutant PFOA (perfluorooctanoic acid) is also used in the synthesis of PTFE and there are some reports where PFOA was detected in the gas phase released from the cooking utensils under normal cooking temperatures (Sajid and Ilyas, 2017).

2.1.2. *Encapsulae S.l*

Encapsulae S.l. is a spin-off technology-based company of the Institute of Ceramics and Glass, a research centre of the Spanish National Research Council (CSIC). The company develops, produces and markets active food packaging that is intended to improve food safety, to extend food self-life and to accelerate biopolymer biodegradation when the packaging is discarded after use. The company detects an opportunity in relation to active food packaging that prevents infection by food insect pests. The material provided by the company and assessed for this case study is made of nanodrops of essential oil anchored to the surface of nano clays and encapsulated in a polymeric film. Specifically, this innovative product must also satisfy food contact regulatory and biodegradation issues. This innovative material is a substitute for Low Density Polyethylene (LDPE) and it's produced to develop food packaging to keep the packaged food free of insect pests. Indeed, it is well known that the incorporation of essential oil in thermoforming polymers is not possible because the process temperatures used in forming are higher than the decomposition temperatures of essential oils. Moreover, the polymer originated from non-renewable sources as fossil fuels are not able to be biodegraded in compost after packaging disposal. Therefore, in addition of the new functionality the industries are currently searching for ways to substitute LDPE food packaging for safer and more sustainable alternatives. The material produced by the company consist in a MCNM of nanodrops of essential oil (clove oil food grade) anchored on the nanoclays (E−558 bentonite clay as layered nanoclay; E−562 sepiolite as fibrillary nanoclays) that are first encapsulated by and organic acid (E−297 Fumaric acid) and therefore incorporated into the polymeric matrix (second encapsulation) during the thermoforming of the food packaging (Salgado et al., 2023 Patent application: EP23382230.3). All the components of the MCMM are based on food grade or food additive materials and the process is free of other chemicals or solvents that are not allowed in the food contact regulation.

The considered benchmark is LDPE, the most common packaging material used for packaging a wide range of products (Veethahavya et al., 2016). LDPE is defined by a density range of 0.910–0.940 g/cm3 and it can withstand temperatures of 80 °C continuously and 95 °C for a short time. LDPE is quite flexible and tough, indeed, it is used to package foods, milk, agricultural products, shrink-wrapping, electronic goods, vehicles, and so on (Veethahavya et al., 2016).

3. Results

The developed approach aims to increase the safety and sustainability of advanced materials without compromising their technological functionality. To ensure this, a life cycle thinking approach (LCT) has been adopted to consider each life cycle stage of a product. A key benefit of LCT is that it allows manufacturers and policymakers to identify opportunities for improvements across the supply chain and in any of the product life cycle stages (Jantunen et al., 2018). Moreover, since the

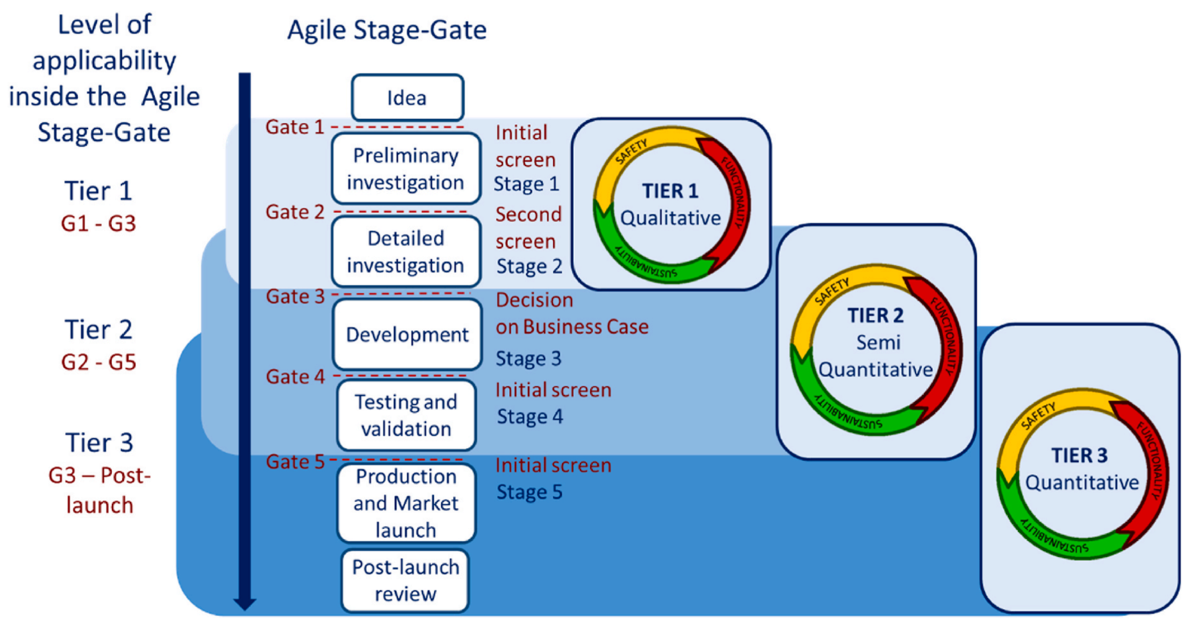

Fig. 2. SSbD tiered assessment proposed in the SUNSHINE project. 'Level of applicability' means at which gate of the stage-gate the approach can be applied.

newly designed materials/products should be simultaneously safe, functional, and sustainable, our approach aims to integrate the evaluation of safety, sustainability, and functionality, rather than treating those as independent parameters. This evaluation of the safety-sustainability-functionality balance of the materials/products should be performed at each stage of the innovation process, so that potential concerns are detected and addressed early enough before the product development reaches a point of no return.

The R&D stage is the most relevant from SSbD perspective because, at this stage, there is a great influence on the product's safety and functionalities, and on the properties determining its environmental impacts later in the lifecycle (i.e., during Use and End of Life) (McAloone and Bey, 2009). In the R&D stage, products can be changed and modified according to safety and sustainability strategies relatively easily and inexpensively (Salieri et al., 2021; Tavernaro et al., 2021) while for the other life cycle stages, the SSbD approach can support the identification of specific safety, sustainability and functionality issues that need to be addressed. However, one important challenge for implementing SSbD approaches in the R&D phase remains the lack of means (e.g., predictive tools) to generate and integrate data/knowledge regarding the safety, sustainability performance and functionality of the newly developed MCNM.

The proposed SSbD approach is implemented in three main levels of assessment as reported in Fig. 2. It is a tiered approach with each tier increasing the complexity of the employed assessment methods as well as the time, resources, data and level of expertise required for their application. Hence, the first level evaluates the safety and sustainability through qualitative methods (Tier 1), the second one with semi-quantitative methods (Tier 2) and the third one with quantitative methods (Tier 3). Tiers 1 and 2 are applied at the screening level in the early stages of innovation, while Tier 3 at a more advanced level when the products are already developed and are ready to be released on the market. The proposed SSbD tiered approach has been aligned to the *Agile Stage-Gate* innovation model (Cooper, 2014; Cooper and Sommer, 2018). Agile Stage-Gate is a standard industrial approach that divides the innovation process into five Stages and requires analysis at each Gate to inform decisions on: (1) Termination if the technical or commercial probability of success are compromised, or if the EHS risks are considered unacceptable; (2) Stage reiteration to improve the safety, performance and/or sustainability of the material/product being developed; or (3) progression to the next Stage if those are in the desired ranges. In this way the Agile Stage-Gate approach continuously challenges the early stages of innovation to cost-efficiently develop safer, functional and more sustainable products.

Specifically, **Tier 1** involves qualitative self-assessment analysis by the industry at the very early stages of the innovation process that aims to identify hotspots (i.e., the sources of potential impacts, such as the emissions to air, along the life cycle) of possible safety and/or sustainability issues to take actions before more resources are invested into further developing the product. Hence, a questionnaire for pre-evaluation of safety, sustainability and functionality is proposed which can be applied to qualitatively assesses possible design alternatives (that are hypothesised or known to be technologically functional) to inform the selection of best options for developing safer and more sustainable materials/products. For the **safety aspect**, questions have been defined according to the steps of the risk assessment methodology, which includes hazard identification, exposure assessment and risk characterization. Specifically, information about toxicity, genotoxicity, toxicokinetic needs to be investigated for advanced materials according to EFSA guidance (Scientific Committee et al., 2021). Also, on the basis of the substance evaluation process of the REACH Regulation (ECHA, Substance evaluation – CoRAP, n.d.), it is possible to identify which "Initial grounds of concern" (e.g., suspected carcinogenic, other hazard based concern, consumer use, exposure of workers etc) can influence the hazard to human health and environment and therefore needs to be investigated. Concerning the **environmental sustainability**, questions were defined according to the "environmental impact categories" used within the LCA methodology, as indicators of specific impacts on the environment (e.g., global warming potential, acidification of soils and water, depletion of natural non-fossil resources, etc.). For **social sustainability** questions were asked according to the social impact categories, which are used with S-LCA methodology to quantitatively investigate the social impacts of organizations and products. For **economic sustainability** questions were proposed with the aim of understanding if the necessary information to perform an LCC is available for the product under assessment. Finally, for the **functionality aspect**, questions were defined with the goal of identifying characteristics making a product functional by their design. Indeed, functional design is the process to formulate a unique design problem by mapping customer needs onto a set of functional requirements (Liu and Lu, 2020).

As a life cycle thinking approach is adopted, the safety, sustainability and functionality assessment is carried out by considering all life cycle

Table 2
Aspects, Indicators and Questions related to the Raw materials and resources stage and their application to the case studies.

Aspects	Indicators	Questions	Laurentia		Encapsulae	
			Innovative	Benchmark	Innovative	Benchmark
Safety	Chemical components included in authoritative lists	Are any of the chemical components used to produce the MCNM* included in any authoritative lists of restricted and hazardous chemicals (e.g. candidate list of SVHC according to Article 57 of REACH)?	NO	YES	NO	NO
	Carcinogenic raw materials	Are any of the raw materials carcinogenic?	NO	YES	NO	NO
	Genotoxic raw materials	Are any of the raw materials genotoxic (mutagenic)?	NO	YES	NO	NO
	Toxic raw materials	Are any of the raw materials toxic to reproduction?	NO	YES	NO	NO
	Endocrine disrupting properties raw materials	Do any of the raw materials have endocrine disrupting properties relevant to human health?	NO	YES	NO	NO
	Respiratory sensitiser raw materials	Are any of the raw materials a respiratory sensitiser?	YES	YES	YES	NO
	Specific target organ toxicity raw materials	Do any of the raw materials have specific target organ toxicity?	YES	YES	NO	NO
	Immunotoxic raw materials	Are any of the raw materials immunotoxic?	I don't know	YES	NO	NO
	Neurotoxic raw materials	Are any of the raw materials neurotoxic?	I don't know	YES	NO	NO
	Skin sensitiser raw materials	Are any of the raw materials a skin sensitiser?	YES	YES	YES	NO
	Raw materials that have adverse effects on eye/skin	Do any of the raw materials have adverse effects on eye/skin (e.g. eye damage/irritation, skin corrosion/irritation)?	YES	YES	YES	NO
	Acute toxicants raw materials	Are any of the raw materials acute toxicants?	YES	YES	NO	NO
	Persistent raw materials	Are any of your raw materials persistent, mobile and toxic (PMT) or very persistent and mobile (vPvM)?	NO	YES	NO	NO
	(Acute) ecotoxic raw materials	Are any of the raw materials (acute) toxic to the environment?	I don't know	YES	NO	NO
	(Chronic) ecotoxic raw materials	Are any of the raw materials (chronic) ecotoxic?	I don't know	YES	NO	NO
	Hazardous for the ozone layer raw materials	Are any of the raw materials hazardous for the ozone layer?	NO	YES	NO	NO
	Bioaccumulative raw materials	Are any of your raw materials bioaccumulative?	NO	YES	NO	NO
	Endocrine disrupting properties raw materials	Do any of the raw materials have endocrine disrupting properties relevant to environment?	I don't know	YES	NO	NO
	hysical hazard properties raw materia	Do any of the raw materials have physical hazard properties (explosive, flammable, corrosive, etc.)?	YES	NO	NO	NO
	Fiber like raw materials	Do any of your raw materials contain fibre like materials (i.e aspect ratio >= 3)	NO	NO	NO	NO
Environment sustainability	Critical materials	Are critical materials used? See EU List	YES	YES	NO	NO
	Use of raw materials derived from renewable resources	Do you use renewable raw materials?	NO	NO	NO	NO
Social sustainability	Material resources access	Do your suppliers respect and protect community access to local material resources (i.e., water, land, mineral, and biological resources) and infrastructure (i.e., roads, sanitation facilities, schools, etc.)?	I don't know	I don't know	YES	I don't know
	Health and safety improvement	Does the activity contribute to improvements to (e.g., through sharing health services) the safety and health of the local community?	I don't know	I don't know	I don't know	I don't know
	Health and safety improvement	Does the activity contribute to damage (e.g., use of hazardous materials, pollution) to safety and health of the local community?	NO	YES	I don't know	I don't know
	Traceability of raw materials	Are there policies in place to allow traceability of your raw materials?	NO	NO	YES	YES
	Absence of armed conflicts	Is the origin country of raw materials free from armed conflicts?	I don't know	I don't know	YES	I don't know
	Raw materials coming from underdeveloped, developing or third world countries	Are there restrictive procedures to minimise social issues (e.g., child labour, political or demographic problems, poor working conditions, forced labour, unfair salary, inequality. etc)?	YES	I don't know	I don't know	I don't know
Economic sustainability	Direct costs for raw material	Can you provide the costs of your raw materials?	YES	I don't know	I don't know	YES
	Direct costs of transportation for raw materials	Can you provide the costs of the transport of your raw materials?	YES	I don't know	YES	YES

stages: from raw materials acquisition up to the End of Life (e.g., recycling, incineration).

Then, in **Tier 2** a (semi)quantitative analysis is performed by a scoring procedure to understand in more detail if the issues identified in the Tier 1 pre-screening have been resolved and if new issues can be identified based on more detailed information. Some examples of methodologies and tools that can be applied in this Tier are NanoRiskScreen (Hristozov et al., 2014) available at nanoriskscreen.greendecision.eu and the Socio-Economic Life Cycle-Based Framework for Safe and Sustainable Design of Engineered Nanomaterials and Nano-Enabled Products (Stoycheva et al., 2022). However, additional research efforts are needed in this tier to develop suitable tools to cover all relevant SSbD aspects as well as (semi)quantitative scoring methodologies to assess and integrate the health, environmental, social, and economic impacts of the materials.

Tier 3 involves a quantitative assessment of safety and sustainability for those design alternatives that were selected in the prior tiers and are ready to be scaled up and released on the market (Gate 5). This more detailed analysis involves regulatory risk assessment as well as Environmental Lifecycle Analysis (E-LCA), Social Environmental Lifecycle Analysis (S-LCA) and Lifecycle Costing (LCC) studies. Technological functionality should always be in commercially viable ranges at this Gate, so it is not part of the Tier 3 assessments.

The proposed SSbD approach is always comparative as it enables to assess if a modified MCNM or the respective product performs better in terms of safety, functionality and sustainability performance than another SSbD design alternative or than a conventional material/product that has the same or a similar function.

Some SSbD approaches are already available in literature for the higher tiers. These have been applied to assess the sustainability of

Table 3
Aspects, Indicators and Questions related to the Production of the MCNM stage and their application to the case studies.

Aspects	Indicators	Questions	Laurentia		Encapsulae	
			Innovative	Benchmark	Innovative	Benchmark
Safety	Chemical components included in authoritative lists	Is the MCNM* in any authoritative lists of restricted and hazardous chemicals (e.g. candidate list of SVHC according to Article 57 of REACH)?	NO	YES	NO	NO
	Carcinogenic MCNMs	Is the MCNM* carcinogenic?	NO	YES	NO	NO
	Genotoxic MCNMs	Is the MCNM* genotoxic (mutagenic)?	NO	YES	NO	NO
	Toxic MCNMs	Is the MCNM* toxic to the reproduction?	NO	YES	NO	NO
	Endocrine disrupting properties MCNMs	Does the MCNM* have endocrine disrupting properties relevant to human health?	NO	YES	NO	NO
	Respiratory sensitiser MCNMs	Is the MCNM* a respiratory sensitiser?	YES	YES	YES	I don't know
	Specific target organ toxicity MCNMs	Does the MCNM* have any specific target organ toxicity?	YES	YES	NO	I don't know
	Immunotoxic MCNMs	Is the MCNM* immunotoxic?	I don't know	YES	NO	I don't know
	Neurotoxic MCNMs	Is the MCNM* neurotoxic?	I don't know	I don't know	NO	I don't know
	Skin sensitiser MCNMs	Is the MCNM* a skin sensitiser?	I don't know	yes	YES	I don't know
	MCNMs that have adverse effects on eye/skin	Does the MCNM* have adverse effects on the eye/skin (e.g. eye damage/irritation, skin corrosion/irritation)?	YES	YES	YES	I don't know
	Acute toxicants MCNMs	Does the MCNM induce acute toxicity?	YES	YES	NO	I don't know
	Persistent MCNMs	Is the MCNM* persistent, mobile and toxic (PMT) or very persistent and mobile (vPvM)?	NO	YES	NO	I don't know
	(Acute) ecotoxic MCNMs	Does the MCNM* induce any acute environmental toxicity?	I don't know	YES	NO	I don't know
	(Chronic) ecotoxic MCNMs	Does the MCNM* induce any chronic environmental toxicity?	I don't know	YES	NO	I don't know
	Hazardous for the ozone layer MCNMs	Is the MCNM* hazardous to the ozone layer?	I don't know	I don't know	NO	NO
	Bioaccumulative MCNMs	Is the MCNM bioaccumulative?	I don't know	YES	NO	I don't know
	Endocrine disrupting properties MCNMs	Does the MCNM* have endocrine disrupting properties relevant to environment?	I don't know	YES	NO	I don't know
	Physical hazard properties MCNMs	Does the MCNM* have any physical hazard properties (explosive, flammable, corrosive, etc.)?	YES	NO	NO	YES
	Fibre like MCNMs	Is the MCNM* a fibre like materials (i.e high aspect ratio >= 3)	NO	NO	YES	I don't know
	Active routes of exposure for workers	Are there any active routes of exposure for workers that can be expected during the production of the MCNM*?	NO	YES	YES	I don't know
	Occupational exposure and upscaled process	Will occupational exposure increase due to the upscaled process?	YES	YES	YES	I don't know
	Chemical or NM emission	Are there any chemical or NM emissions into the indoor environment?	YES	YES	YES	I don't know
	Dustiness from the production process	Does the production process produce dust?	YES	NO	YES	YES
	Liquid emission from the production process	Does the production process cause leaks or releases of liquids?	YES	YES	NO	NO
	NM emissions into the environment	Are there any chemical or NM emissions into the environment? (wastewater and airborne)	YES	YES	NO	YES
Environment sustainability	Critical materials		NO	YES	NO	YES
	Consumption of water resources in production process	Are you in the process of reducing the water consumption during the production process?	NO	NO	YES	NO
	Increase the yield of your process	Are you in the process of increasing the yield of your process?	NO	NO	YES	NO
	Reduce the use of raw materials	Are you in the process of reducing the raw materials use?	YES	NO	YES	NO
	Impact on climate change from production process	Are you in the process of reducing the greenhouse gases when producing your innovative material?	YES	YES	YES	NO
		Are renewable energy resource used?	NO	NO	NO	NO
	Energy consumption during production process	Are you in the process of reducing the energy consumption when producing your innovative material (for instance considering different temperatures and reduce the pressure)?	YES	YES	YES	NO
	Emissions to water	Are you in the process of reducing the emissions of chemicals and of NM to water generated during the production process?	YES	NO	YES	NO
	Emissions to air	Are you in the process of reducing the emissions of chemicals and of NM to air generated during the production process?	YES	NO	YES	NO
	Waste production during production process	Are you in the process of reducing the waste generated during the production process?	YES	NO	YES	NO
	Reuse of by-product/co-product	Are you in the process of re-use the by-products/co-products generated during the production process?	YES	NO	YES	YES
	Recyclability of waste produced in production process	Are you in the process of recycling the waste produced during the production process?	I don't know	NO	YES	YES
Social sustainability	Health and safety improvement	Does the activity contribute to improvements to the (e.g. through sharing health services) safety and health of the local community?	YES	NO	YES	NO
	Health and safety improvement	Does the activity contribute to damage (e.g. use of hazardous materials, pollution) safety and health of the local community?	NO	NO	NO	NO
	Local employment	Does the organization positively affect the local employment rates?	YES	YES	YES	NO

	Assessment of suppliers	Are suppliers socially responsible (e.g. if they implement CSR principles)?	NO	NO	YES	YES
	Raw materials coming from underdeveloped, developing or third world countries	Are there restrictive procedures to minimise social issues (e.g., child labour, political or demographic problems, poor working conditions, inequality. etc)?	YES	NO	NO	NO
	Technological development, economic impact, education opportunities	Did you consider if the production process results in technological development, additional education opportunities?	YES	NO	NO	NO
Economic sustainability	Direct costs of waste disposal in production	Can you provide and/or estimate the costs of disposable waste during material production?	YES	NO	YES	YES
	Direct costs of maintenance for production	Can you provide and/or estimate the costs of the material production process?	YES	NO	YES	YES
	Direct costs of installation (heating, lighting) for production	Are installation costs expected for implementing SSbD actions?	YES	NO	YES	NO
	Economic benefits of by-product/co-product	Can you sell your by-product/co-product?	NO	NO	NO	NO
	Direct benefits of production	Can you identify direct economic benefits for the innovative material?	YES	Not applicable	YES	NO

** As the questionnaire is of a comparative nature, the term MCNM is considered when assessing the MCNM. The term MCNM is replaced by the term benchmark when the benchmark is assessed*

indigo dyeing color in the fashion sector (Lai and Chang, 2021) or of inhibitors in pharmaceutical products (Romeiro et al., 2019), the design of cellulosic bioelectricity supply chain networks (Yue et al., 2014), the design of a commercial building in Shanghai (Wang et al., 2010) and the sustainability of mechatronic systems application to a regenerative braking system (Mehdi and Boudi, 2021). In the case of lower tiers of assessment few methodologies are available, one examples is the one developed by (Schmidt Rivera et al., 2019) for innovative and sustainable food packaging.

Here, the focus is presenting the Tier 1 SSbD methodology of the proposed developed approach which is intended for the earliest stages of material/product design and consists of a self-assessment qualitative questionnaire, which was created for material/product developers and manufacturers from industry to pre-evaluate specific sustainability, safety and functionality aspects. The questionnaire is particularly suited for SMEs as it requires entry level expertise to complete. In this manuscript it is demonstrated in two case studies provided by the industrial company Laurentia, i.e., PFAS-free anti-sticking coating used in baking trays and molds and by Encapsulae, i.e., nanodrops of essential oil anchored at the surface of nanoclays and encapsulated in a polymeric film.

3.1. SSbD approach Tier 1: self-assessment questionnaire

The developed questionnaire is divided in four parts, where the **first part** is an introduction to the proposed SSbD approach and explains the goal and scope of the survey, as reported in Annex 1 of Supplementary Information.

The **second** part (Table 1 in Supplementary Information) consists of general questions related to both, the MCNM and the respective product. These questions investigate the products' functionality, the sector of application and identify a benchmark against which the assessed product can be compared. These questions are intended to obtain a general idea of the target material/product and to pinpoint to possible hotspots (sources) of potential health or environmental impacts. These hotspots would then be assessed in more detail in the later Tiers 2 and 3.

The **third part** of the questionnaire (Table 2 in Supplementary Information) is aimed at collecting a set of information about the MCNM and the product incorporating the MCNM that are eventually available in the R&D stage and are divided according to the following life-cycle stages: Raw materials/production, use and End of Life.

As reported in Table 2 of the Supplementary Information, in the production stage of the material/product, the requested information is aimed at identifying those hotspots that can cause impacts on the environment and on human health.

Specifically, inputs, such as chemicals, energy sources, and water use, and the outputs, such as waste, and emissions are required, since they can cause impacts in terms of global warming, eutrophication, acidification of water, etc., with an inevitable negative effect on human health and the environment. Furthermore, additional questions are asked to obtain information on aspects of sustainability and functionality such as for example the recycling/re-use options within a circular economy perspective or key critical quality attributes, and the yield of the production process. The questions related to the Use stage are asked to understand the lifetime of the material/product, if the company is aware of how it wants to increase their sustainability during the Use stage, and who is the final client/customer. Finally, the questions related to the End of Life are asked to understand both, if the company has considered the idea of producing biodegradable, recyclable, and reusable materials/products, if transformation are expected during the End of Life and if the company has considered different End of Life (EoL) alternatives.

The second and third part of the questionnaire are not comparative, indeed their aim is not to compare the designed alternatives but to help the user to collect the data needed to fulfil the fourth part of the questionnaire. Accordingly, the structure of these two parts is the same of the fourth.

Finally, the **fourth** part of the questionnaire is more specific and includes a set of detailed questions that need to be considered during the R&D stage. The possible answers to each question are "Yes", "No", "I don't know" and "Not applicable". The assessment is performed by comparing either the material/product against a benchmark (i.e., another existing material/product which has the same function) or comparing alternative modification options (e.g., different coatings).

This part is divided into five sections which represent the five LCS assessed during the R&D stage: 1) Raw materials and resources needed to produce the material/product, 2) Production of the MCNM, 3) Production of the product incorporating the MCNM, 4) Use of the product, and 5) End of Life treatment. This subdivision was made to obtain information on all phases of the product life cycle, starting from the extraction of raw materials, up to the EoL management. For each of the five LCS, the set of questions/issues to be addressed are divided according to the following classifications: the aspects to be considered (e.g., safety, functionality and economic, environmental and social aspects) and the indicators and the questions used to measure the fulfilment. In the next sections, the detailed description of the **fourth** part of the questionnaire is presented for each lifecycle stage.

3.1.1. Raw materials and resources

This section shows how the stage of raw materials and resources is addressed and considered within the SSbD approach for the case studies at hand. There are thirty questions in this section, twenty for the first group (safety) and ten for the second group (sustainability) (Table 2).

Table 4
Aspects, Indicators and Questions related to the Production of the product incorporating the MCNM stage and their application to the case studies.

Aspects	Indicators	Questions	Laurentia		Encapsulae	
			Innovative	Benchmark	Innovative	Benchmark
Safety	Active routes of exposure for workers	Are there any active routes of exposure for workers that can be expected during the production of the product incorporating the MCNM*?	YES	YES	YES	YES
	Occupational exposure and upscaled process	Will the occupational exposure increase due to the upscaled process?	YES	YES	YES	YES
	Chemical or NM emission	Are there any chemical emissions into the indoor environment?	YES	YES	YES	YES
	Dustiness from the production process	Does the production produce dustiness?	NO	YES	YES	YES
	Liquid emission from the production process	Does the production process emit liquid emission?	NO	YES	YES	NO
	Release of bioaccumulating substances	Does your production process release bioaccumulating substances?	NO	YES	YES	YES
	Exposure reduction measures	Do you put in place exposure reduction measures to produce the product incorporating the MCNM*?	YES	YES	YES	NO
	Release of persistent substances	Does your production process release persistent substances?	NO	YES	NO	NO
	Release of carcinogenic substances	Does your production process release carcinogenic substances?	NO	YES	NO	NO
	Release of suspected carcinogenic substances	Does your production process release suspected carcinogenic substances?	NO	YES	NO	NO
	NM emissions into the environment	Are there any chemical or NM emissions into the environment?	NO	YES	NO	NO
Environment sustainability	Consumption of water resources in manufacturing	Are you in the process of reducing the water consumption during manufacturing?	Not applicable	NO	YES	NO
	Impact on climate change (LCA midpoint) from manufacturing and production process	Do you use renewable energy resource during manufacturing?	I don't know	NO	NO	NO
	Impact on climate change from manufacturing	Are you in the process of reducing the emission of greenhouse gases when designing your innovative product?	YES	Not applicable	YES	YES
	Energy consumption during manufacturing	Are you in the process of reducing energy consumption when designing your innovative product?	YES	Not applicable	YES	NO
	Emissions to water	Are you in the process of reducing emissions of chemicals and of NM to water generated during manufacturing?	YES	NO	YES	NO
	Emissions to air	Are you in the process of reducing emissions of chemicals and of NM to air generated during manufacturing?	YES	NO	YES	NO
	Waste production during manufacturing	Are you in the process of reducing the waste generated during manufacturing?	YES	YES	YES	NO
	Reuse of by-product/co-product	Can you re-use or sell the by-product/co-product generated during the production process?	NO	NO	NO	NO
	Recyclability of waste produced in manufacturing	Are you in the process of making recyclable the waste produced during the manufacturing be recycled?	I don't know	NO	YES	YES
Social sustainability	Local employment	Does the organization positively affect the local employment rates?	NO	YES	YES	NO
	Assessment of suppliers	Are suppliers socially responsible (e.g., if they implement CSR principles)?	YES	YES	YES	NO
	Raw materials coming from underdeveloped, developing or third world countries	Are there restrictive procedures to minimise social issues (e.g., child labour, political or demographic problems, forced labour, unfair salary, poor working conditions, inequality. etc)?	YES	YES	I don't know	NO
	Technological development, economic impact, education opportunities	Did you consider if the manufacturing process results in technological development, additional education opportunities?	YES	YES	YES	NO
Economic sustainability	Direct costs of waste disposal in manufacturing	Can you provide the costs of disposal of waste during product manufacturing?	YES	NO	YES	YES
	Direct costs of water treatment for manufacturing	Can you provide the costs of water treatment for product manufacturing?	YES	NO	YES	YES
	Direct costs of maintenance for manufacturing	Can you provide the costs of the maintenance for product manufacturing?	YES	NO	YES	YES
	Direct costs of installation (heating, lighting) for manufacturing	Are installation costs expected for implementing SSbD actions?	YES	YES	YES	YES
	Direct benefits of product	Can you identify direct economic benefits for the innovative product?	YES	Not applicable	YES	YES

3.1.2. *Production of material*

This section shows how the stage of the Production of MCNM is addressed and considered within the SSbD approach. As reported in Table 3, there are forty-nine questions, twenty-six for the first group (safety) and twenty-three for the second group (sustainability).

3.1.3. *Manufacturing of the product*

This section shows how the stage of the production of the product that incorporates the MCNM is addressed and considered within the SSbD approach. As reported in Table 4., the questionnaire contains twenty-nine questions, eleven for the first group (safety) and eighteen for the second group (sustainability).

3.1.4. *Use of the product*

This section shows how the stage of the use of the product incorporating the MCNM is addressed and considered within the SSbD approach, assuming that the MCNM does not have a use without being incorporated in a product. In the cases when the MCNM have a use without being incorporated in a product, the provided questions can be adapted to the specific case. As reported in Table 5, there are forty-two questions in this section, nine for the first group (safety), thirteen for the second group (sustainability) and twenty for the third group (functionality).

Table 5
Aspects, Indicators and Questions related to the Use of the product stage and their application to the case studies.

Aspects	Indicators	Questions	Laurentia		Encapsulae	
			Innovative	Benchmark	Innovative	Benchmark
Safety	Release of materials/substances that look like asbestos	Does your product release materials/substances that are fibre like (i.e., aspect ratio >= 3)	NO	NO	NO	NO
	Release of persistent substances	Does the product incorporating the MCNM release persistent substances during the use phase?	NO	NO	NO	NO
	Release of carcinogenic substances	Does the product incorporating the MCNM release carcinogenic substances during the use phase?	NO	NO	NO	NO
	Release of suspected carcinogenic substances	Does the product incorporating the MCNM release suspected carcinogenic substances during the use phase?	NO	NO	NO	NO
	Release of bioaccumulating substances	Does the product incorporate the MCNM release bioaccumulating substances during the use phase?	NO	NO	NO	NO
	Chemical or NM emission	Are there any release of MCNM* or of chemical into the environment?	NO	NO	NO	NO
	Physical hazard properties MCNMs	Does the product have any physical hazard properties (explosive, flammable, corrosive, etc.)?	NO	NO	YES	YES
	Reactivity of the MCNM	Do you expect that the MCNM* could be modified (transformed or degraded) during the use phase?	NO	YES	YES	YES
	Release of MCNM	Do you expect that the MCNM* could be released or dissolved from the matrix during the use stage?	YES	YES	NO	NO
Environment sustainability	Consumption of water resources in product use	Did you consider reducing water consumption when designing the use of your innovative product?	YES	YES	YES	NO
	Impact on climate change from product use	Did you consider reducing the emission of greenhouse gases when designing the use of your innovative product?	YES	YES	YES	NO
	Energy consumption from product use	Did you consider reducing energy consumption when designing the use of your innovative product?	YES	YES	YES	NO
	Emissions to water from product use	Did you consider reducing the emission to water when designing the use of your innovative product?	YES	YES	YES	NO
	Emissions to air from product use	Did you consider reducing the emission to air when designing the use of your innovative product?	YES	YES	YES	NO
	Waste production from product use	Are you in the process of reducing the waste generated during the product use?	YES	NO	YES	YES
	Less waste, less use of plastic in product use	Are you in the process of reducing the amount of packaging?	YES	NO	NO	NO
	Use of bio-based materials	Can you use bio-based packaging?	I don't know	I don't know	YES	NO
	Repairability of product	Can the product be easily repairable?	YES	YES	NO	NO
	Reuse of chemical substances in product	Can the product be easily reused?	YES	YES	NO	YES
	Recyclability: use of recycled raw materials and production of a recyclable innovative product	Can the product be recycled after use?	YES	YES	NO	YES
		Can the product be dismantled and separated to allow recycling of aspects of the product?	YES	YES	NO	NO
Economic sustainability	Direct benefits of use of product	Are there any direct economic benefits in using the innovative product?	YES	Not applicable	YES	NO
Functionality	Durability	Is the MCNM* designed to have improved durability (the ability to remain functional)?	YES	YES	YES	NO
	Performance	Is the MCNM* designed to have improved performance (the action or process of performing a task or function)?	YES	YES	YES	NO
		Is the MCNM* designed to have an improved incorporating process (easier interaction with matrix, easier applicability, easier processing)?	YES	YES	YES	NO
	Reliability	Is the MCNM* designed to have an improved reliability (the quality of performing consistently well)?	YES	YES	YES	NO
	Useability	Is the MCNM* designed to have an improved useability (the quality or state of being usable)?	YES	YES	YES	NO
	Versatility	Is the MCNM* designed to be versatile (the quality to be used for different purposes)?	YES	YES	YES	NO
	Customer needs	Have customer needs been mapped?	YES	YES	YES	YES
	Target customer	Did you identify the target customer for the MCNM*?	YES	YES	YES	YES
	Process scalability	Can the design process phase be easily upscaled?	YES	YES	YES	NO
		Can the incorporating process phase be easily upscaled?	YES	YES	YES	NO
	Durability	Is the product incorporating the MCNM* designed to have an improved durability (the ability to remain functional)?	YES	YES	YES	NO
		Do you expect that the MCNM *could be modified during the USE phase (dissolution, release, agglomeration, surface reactivity)?	YES	YES	YES	NO
		Do you expect that the MCNM* surface modifications could affect functionality?	YES	YES	YES	NO
	Performance	Is the product incorporating the MCNM* designed to have an improved performance (the action or process of performing a task or function)?	YES	YES	YES	NO
	Reliability	Is the product incorporating the MCNM* designed to have an improved reliability (the quality of performing consistently well)?	YES	YES	YES	NO
	Useability	Is the product incorporating the MCNM* designed to have an improved useability (the quality or state of being usable)?	YES	YES	YES	NO
	Versatility	Is the product incorporating the MCNM* versatile (the quality to be used for different purposes)?	YES	YES	YES	NO
	Customer needs	Have customer needs been mapped?	YES	YES	YES	YES
	Target customer	Did you identify the target customer for the product MCNM*?	YES	YES	YES	YES
	Service issues	Can you identify any service issues (e.g., lower performances of the product) related to the product incorporating the MCNM*?	YES	YES	YES	YES

Table 6
Aspects, Indicators and Questions related to the End-of-Life stage and their application to the case studies.

Aspects	Indicators	Questions	Laurentia		Encapsulae	
			Innovative	Benchmark	Innovative	Benchmark
Safety	Worker's exposition	Are workers exposed to MCNM* (i.e., via inhalation)?	NO	NO	NO	NO
	MCNM emission	Are there any expected MCNM *emissions into the environment?	YES	NO	NO	NO
Economic sustainability	Direct costs of end-of-life	Can you estimate the costs for the end-of-life scenarios of the innovative product?	I don't know	I don't know	YES	YES
Social sustainability	End-of-life information	Is there clear guidance on the end of life-options provided through labelling?	NO	NO	NO	NO

3.1.5. *End of life*

This section shows how the stage of the end of life of the product incorporating the MCNM is addressed and considered within the SSbD approach. As reported in Table 6, there are four questions in this section, two for the first group (safety) and two for the second group (sustainability).

3.2. *Comparing SSbD alternatives and dealing with uncertainty*

As already stated, the possible answers to each question are "Yes", "No", "I don't know" and "Not applicable". The assessment is performed by comparing either the material/product against a benchmark (i.e., another existing material/product which has the same function) or comparing alternative modification options (e.g., different coatings).

Basing on the type of question, "Yes" and "No" answers are associated to positively or negatively contributing to safety and sustainability, e.g., answering "Yes" to "Are any of the raw materials carcinogenic?" results in a negative contribution as opposed to answering "Yes" to "Do you use renewable raw materials?" which results in a positive contribution. The aim of the questionnaire is to establish which of the compared alternatives have the highest number of answers with positive contribution to sustainability regardless of the actual "Yes" or "No" answer.

This simple comparison is complicated by the presence of uncertain

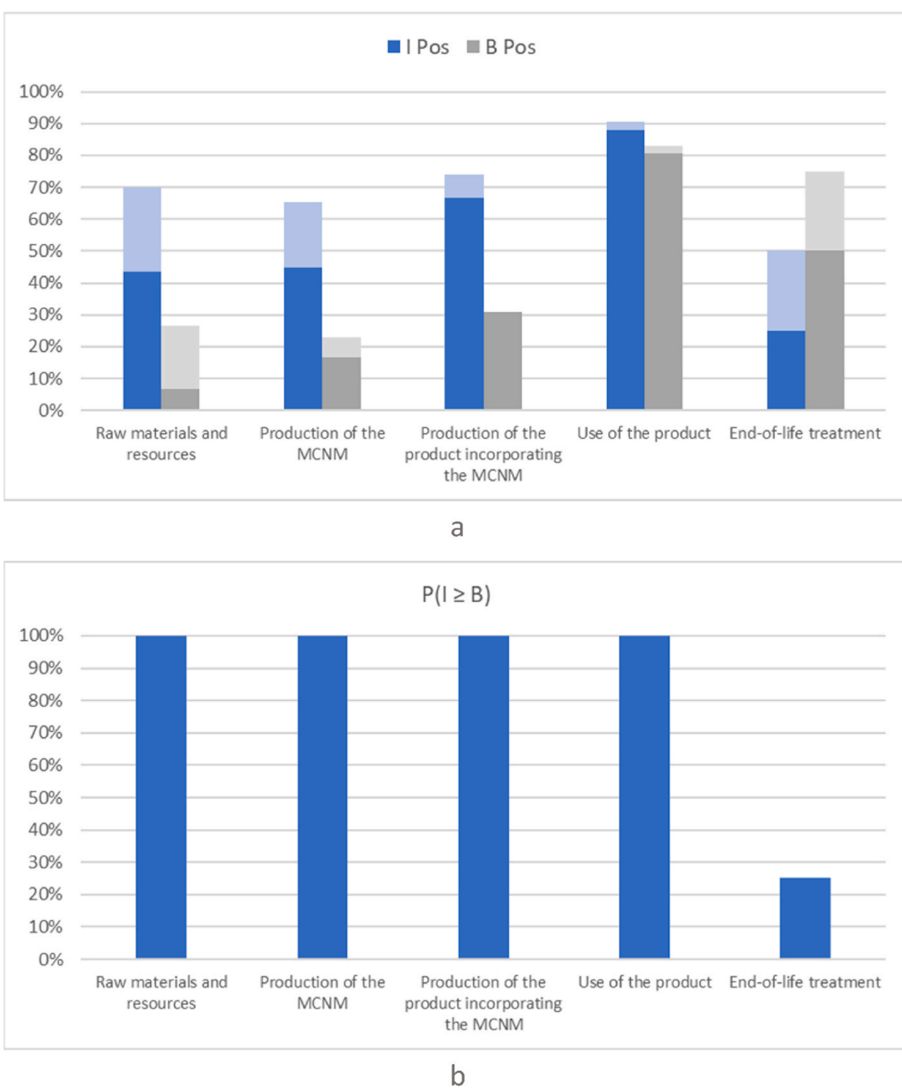

Fig. 3. Laurentia case study (a) Percentage of positive contributions by life cycle stages; (b) Probability that the innovative MCNM is better or equal than the benchmark for each life cycle stages. I Pos = positive contributions for the Innovative material; B Pos = positive contributions for the benchmark. Life cylcle stages: Raw materials and resources needed to produce the material/product, Production of the MCNM, Production of the product incorporating the MCNM, Use of the product, and End of life treatment. The light blue and light grey parts of the column show the relative uncertainty for both the innovative MCNM and the benchmark. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

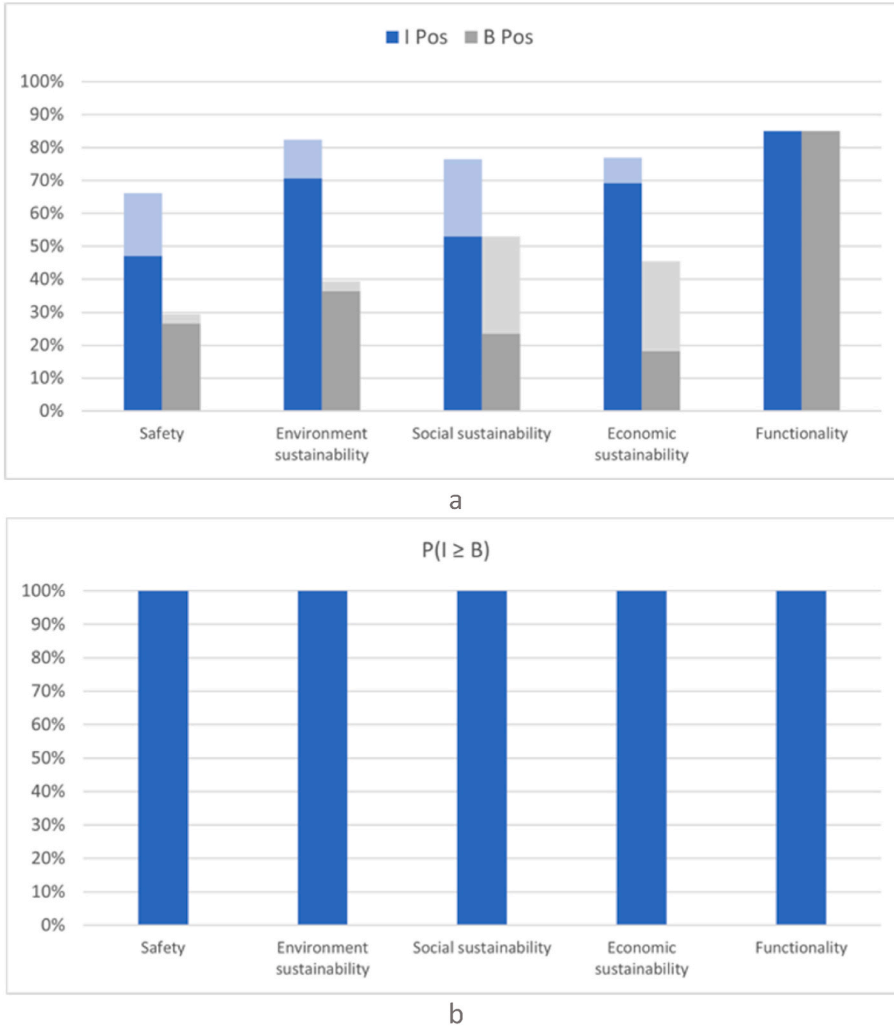

Fig. 4. Laurentia case study (a) Percentage of positive contributions by aspects; (b) Probability that the innovative MCNM is better or equal than the benchmark for each aspect. The light blue and light grey parts of the column show the relative uncertainty for both the innovative MCNM and the benchmark. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

answers (i.e., I don't know) which make the results of the comparison itself uncertain, i.e., it is not possible to state that one solution is contributing to sustainability more than another, but rather that it has a certain probability of doing so. As each uncertain question can only take two possible states, "Yes" or "No", it can be seen as a Bernoulli trial (Proakis, 1985), when considering the whole set of uncertain questions the result's probability distribution is therefore modelled by a binomial distribution (i.e., the probability distribution of a sequence of a specific number of independent Bernoulli trials with fixed success probability). As the aim of the questionnaire is to establish which of the compared alternatives have the highest number of answers with positive contribution to sustainability this implies comparing the results of different Binomial distributions, one for each alternative, and establish how likely it is that one alternative has a higher number of positive contributions than the other. To do so, for each alternative, the starting number of answers with a positive contribution is used as a fixed base upon which the Binomial distribution's possible outcomes are summed. Then, each possible result of the target material/product is compared against each possible result of the other scenarios and the conjunct probabilities of all the pairs of results for which the innovative target alternative beats the other are summed up.

To avoid the possible biases related to the number of 'Not applicable' answers, results are expressed as percentages of positives as opposed to the absolute number of positives. This also allows comparisons between products with a different number of not applicable responses.

The presented methodology has been implemented in a Microsoft Excel tool which automatically compares the alternatives and produces results and charts. The tool will be included into the SUNSHINE SSbD e-infrastructure as a stand-alone assessment module.

The results of the questionaries related to the silica carbide and titanium dioxide (SiC@TiO2) case study are shown in Fig. 3, Figs. 4 and 5, and those related to the nano-drops of essential oil anchored to nano clays surface and encapsulated in a polymeric film are shown in Fig. 6, Figs. 7 and 8. The blue columns report the results for the innovative material, while the grey ones those for the benchmark. The light blue and light grey parts of the column show the relative uncertainty for both the innovative MCNM and the benchmark. This implies that when the actual positives plus the uncertainty of an alternative (i.e. the total height of a column) is below of the actual positives only of another alternative (i.e. the dark colour part only), then, the probability of the latter being better than the former is 100% as even if all the former's uncertain answers would turn into positives they will not ever be higher than the latter.

Specifically, Figs. 3a and 6a show the percentage of positive contributions for the innovative material and the benchmark by life cycle stages (Raw materials and resources needed to produce the material/product, Production of the MCNM, Production of the product incorporating the MCNM, Use of the product, and End of life treatment) and

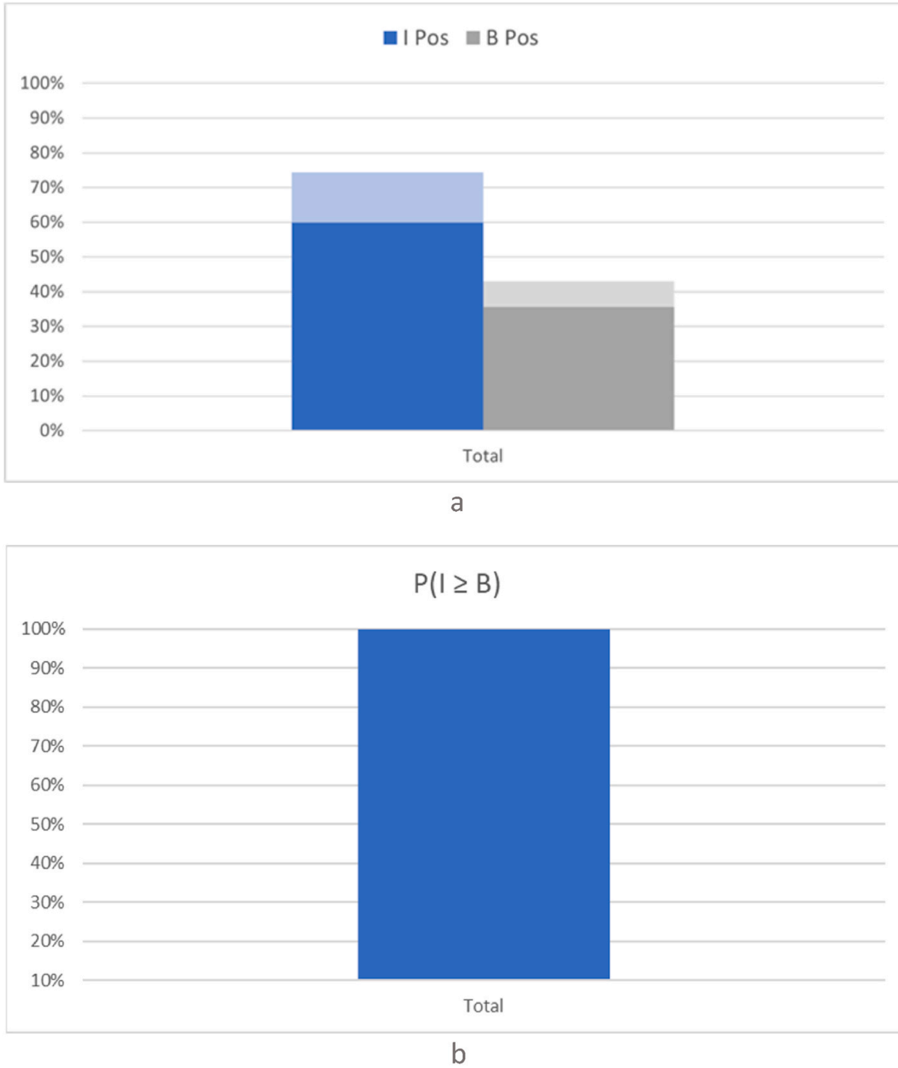

Fig. 5. Laurentia case study (a) Total percentage of positive contributions for the innovative material and the benchmark; (b Probability that the innovative MCNM is better or equal than the benchmark. The light blue and light grey parts of the column show the relative uncertainty for both the innovative MCNM and the benchmark. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Figs. 3b and 6b show the probability, for each life cycle stage, that the innovative MCNM is better or equal than the benchmark. In addition, Figs. 4a and 7a show the percentage of positive contributions for the two assessed materials divided on the basis of the safety, environmental, social and economic sustainability and functionality aspects, while Figs. 4b and 7b shows the probability, for each aspect, that the innovative MCNM is better or equal than the benchmark. Finally, Figs. 5a and 8a show the percentage of positive contributions for the innovative material and the benchmark, while Figs. 5b and 8b show the probability that the innovative MCNM is better or equal than the benchmark.

4. Discussion of the results

A three-tiered approach to support SSbD decision making for advanced materials is presented, each tier increasing the complexity of the employed assessment methods as well as the time, resources, data and level of expertise required for their application. The focus of this manuscript is particularly on the lowest Tier 1 methodology which has been designed for the early stages of product development. It encompasses a questionnaire which supports the assessment of various aspects associated to safety, sustainability and functionality along the lifecycles of advanced materials. It is a first attempt to derive a qualitative self-assessment procedure to be applied in the R&D stage by industries developing MCNMs to assess the safety, sustainability and functionality performances of their materials/products. Additional developments of the proposed questionnaire should therefore include a stakeholder consultation process which should also drive the identification of additional questions to cover aspects which are not considered in this version, the derivation of weights to be associated to the provided questions as well as the development of a different integration methodology tailored on the five steps proposed in (C. Caldeira et al., 2022) and applied in (C. Caldeira et al., 2023). The future developments of the approach will also include "red flags" amongst the list of questions as a basis for "no go" decisions. For example, the question "Does the product incorporating the MCNM release carcinogenic substances during the use phase?" should immediately raise a red flag and will not provide a conclusion of the product being "better" than an alternative irrespective of the number of "yes" answers to other questions.

As far as the derivation of weights is concerned, the Tier 1 screening level methodology needs to be equipped with an advanced scoring procedure that integrates heterogeneous assessment criteria and indicators with stakeholder trade-offs. Additionally, along with the full alignment of Tiers 1–3 to the EC JRC SSbD Framework to enable its practical operationalization for advanced materials, additional work is needed to align the aspects to be assessed along the three tiers in order to guarantee coherence of the assessed aspects.

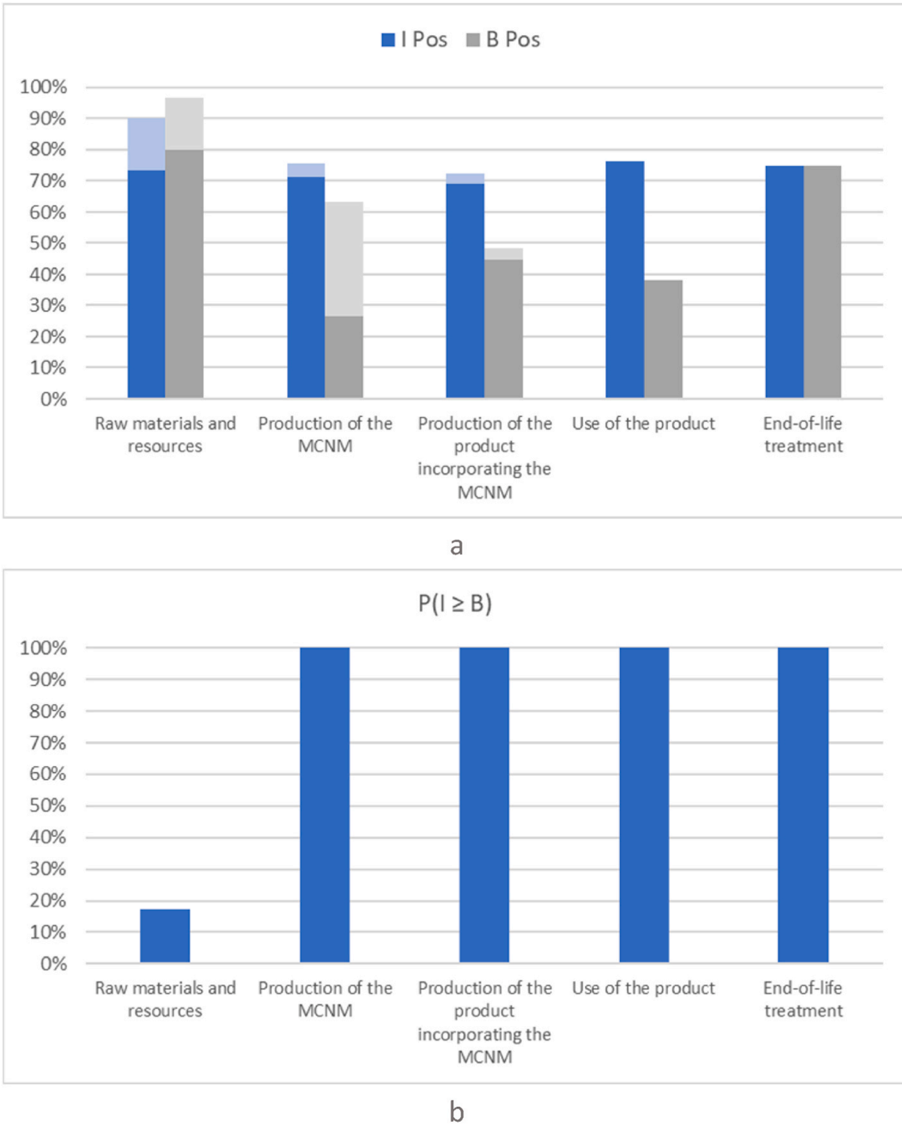

Fig. 6. Encapsulae case study (a) Percentage of positive contributions by life cycle stages; (b) Probability that the innovative MCNM is better or equal than the benchmark for each life cycle stages. I Pos = positive contributions for the Innovative material; B Pos = positive contributions for the benchmark. Life cylcle stages: Raw materials and resources needed to produce the material/product, Production of the MCNM, Production of the product incorporating the MCNM, Use of the product, and End of life treatment. The light blue and light grey parts of the column show the relative uncertainty for both the innovative MCNM and the benchmark. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Moreover, the Tier 1 methodology should be better enabled to account for uncertainties in both input data and integration algorithms. Indeed, the proposed approach only accounts for epistemic uncertainties reflected by the "I don't know" answers to the questions. The uncertainties pertaining to the input data that are propagated through the aggregation algorithms into the final results are not considered in the current version. Similarly, the modelling uncertainties stemming from the algorithms themselves are also not estimated. To partially fill this current gap, we are planning to build a software tool based on the presented approach, which will be equipped with a methodology for probabilistic uncertainty assessment based on the Monte Carlo approach.

The proposed approach is complementary to the Early4AdMa system (Oomen et al., 2022). Indeed, while Early4AdMa has been developed to provide policymakers and regulators the opportunity to anticipate on potential novel risks of materials already on the market, our approach is comparative and is designed to support industries, especially SMEs in selecting safer and more sustainable design alternatives for materials/products that are in the early R&D stages of development. The two approaches are complementary, and their further alignment and possible integration in an overarching SSbD strategic approach is currently being discussed in the OECD WPMN Steering Group on Advanced Materials.

Indeed, the R&D stage is the most relevant in the context of SSbD approaches because, at this stage, safety, sustainability and functionality issues can be addressed and the materials/products being developed can still be modified without incurring excessive costs (Salieri et al., 2021; Tavernaro et al., 2021). In fact, it is during the R&D stage that the potential impacts of the technologies along their lifecycles are investigated and decided. This is thus the stage where the presented Tier 1 questionnaire should be applied using all the available information related to each LCS of the target material/product.

The first part of the questionnaire is an extensive set of general questions for the preliminary evaluation of the target materials/products and the related performances which is needed to properly define the scope and the boundaries of the assessment as well as to accurately evaluate the results provided by the core part of the questionnaire. The latter consists of a set of multiple-choice versatile and intuitive questions which are thought to cover the most relevant aspects to be assessed and where each provided answer is classified as having positive or negative contributions to safety, sustainability and functionality. This assessment can be applied to assess different alternative solutions and provides a comparison score for each solution by summing up the number of positive contributions for each alternative towards a comprehensive assessment of the target materials/products overall performances.

Moreover, the results provided by the Tier 1 assessment support companies to understand which are the life cycle stages that are weaker

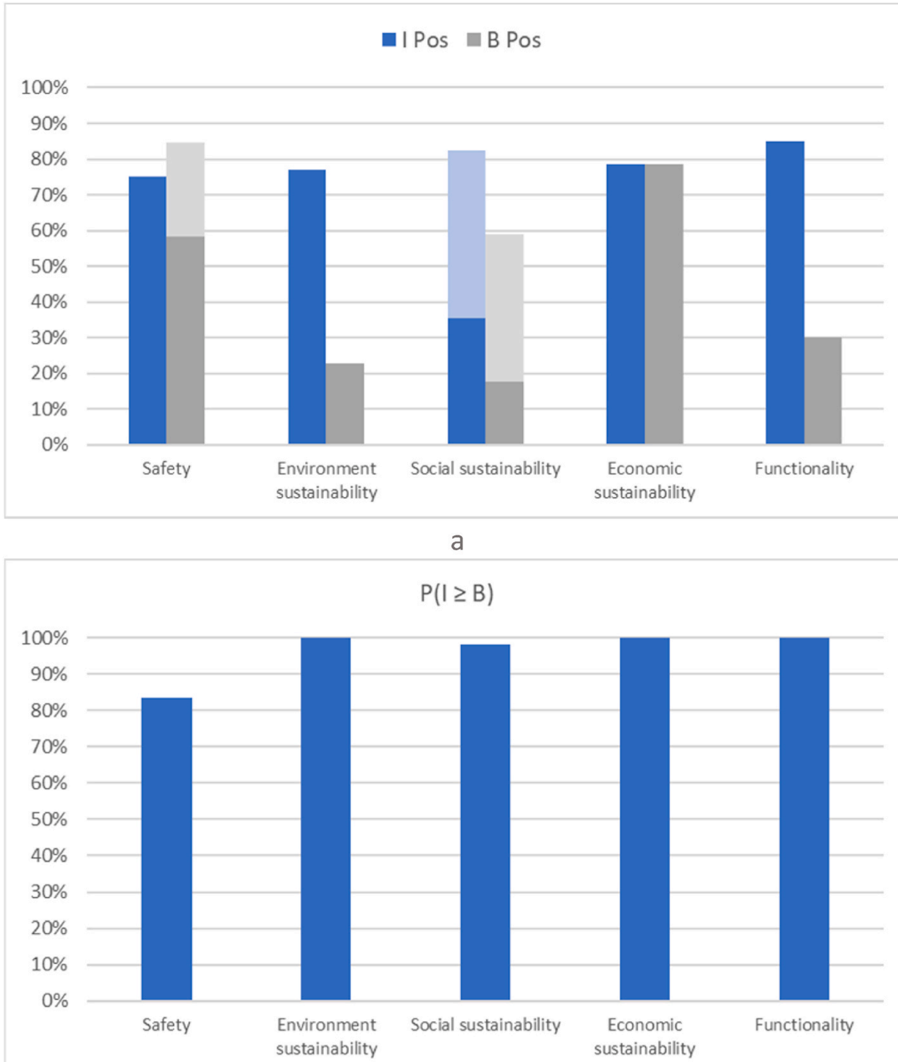

Fig. 7. Encapsulae case study (a) Percentage of positive contributions by aspects; (b) Probability that the innovative MCNM is better or equal than the benchmark for each aspect. The light blue and light grey parts of the column show the relative uncertainty for both the innovative MCNM and the benchmark. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

in terms of safety, sustainability or functionality performance (i.e. lower percentage) or the assessment results that are characterised by high uncertainty (see Figs. 3a, 4a and 6a and 7a). The large number of questions allows evaluation of the assessed aspects from different angles while limiting relevant fluctuations in the case changes are made to the questionnaire, thus leading to solid results. The large number of questions could mean that the questionnaire would be time consuming and require expert input. If this is found to be the case when industrial partners use the tool, simplifications of the questionnaire would be pursued in subsequent versions.

Additionally, it is important to underline that this is a comparative assessment which requires to collect similar information also for the identified alternatives or a benchmark. This applies not only to Tier 1 of the SSbD approach, but also for Tiers 2 and 3. Nevertheless, as this questionnaire is targeted at users from industry, who are expected to have first-hand information about the technologies they are developing as well as about their alternatives, this should not substantially increase the workload or the level of expertise needed to fill the questionnaire.

It is worth noting that the proposed Tier 1 methodology is built on answers which all have the same weights since all questions are supposed to have the same importance. Future developments could be weighted to reflect the different importance of different aspects.

It is important to remember that this is a qualitative assessment which can be affected by the subjective opinions of respondents asked to choose among "Yes", "No", "I don't know" and "Not applicable" answers. There are situations where it is difficult to provide a clear answer and situations that require additional clarifications, but the respondent will always choose one of the pre-defined answers, which contributes to uncertainty in the final results. As already explained above, the developed methodology allows to account for these indeterminate results in the comparison of the assessed scenarios. The results of this Tier 1 methodology should always be seen as a first screening of the assessed materials/products which will be confirmed or denied by the application of Tier 2 and 3 assessments.

As a final general consideration, although the questionnaire has been firstly applied to MCNMs, it includes general questions that can be applied, with slight modifications, to a greater range of materials and products, making it applicable to different sectors.

The added value of this self-assessment methodology was demonstrated through two case studies from the industrial company Laurentia: i.e., PFAS-free anti-sticking coating used on bread baking trays, and Encapsulae: i.e., active food packaging as pest barrier based on nanodrops of essential oil anchored to the surface of nano clays and encapsulated in a polymeric film. These innovative MCNM-based products

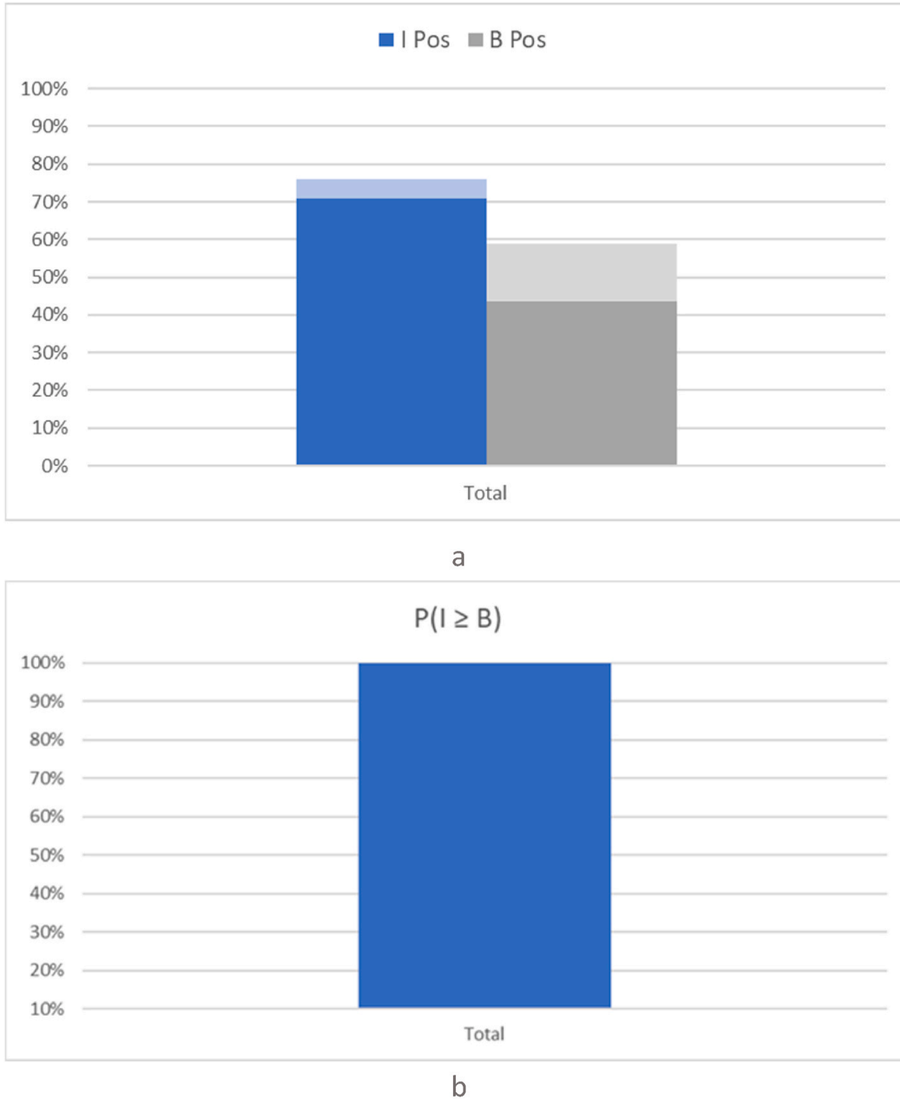

Fig. 8. Encapsulae case study(a) Total percentage of positive contributions for the innovative material and the benchmark; (b Probability that the innovative MCNM is better or equal than the benchmark. The light blue and light grey parts of the column show the relative uncertainty for both the innovative MCNM and the benchmark. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

were compared with their conventional counterparts, that is Teflon (here referred to as benchmark product) for Laurentia and LDPE for Encapsulae. The results of this comparison are reported in Figs. 3, Figs. 4 and 5 for Laurentia case study and Figs. 6, Figs. 7 and 8 for Encapsulae case study. Fig. 3a shows that the innovative coating performs better when considering the overall percentage of positive contributions than the Teflon for four out of the five assessed life cycle stages. In fact, the EoL stage is the only one in which the innovative material has fewer positive contributions than the benchmark. There are not available data in literature for emissions on waste Teflon incineration plants. At lab scales studies about thermal degradation of PTFE (Garcia et al., 2007) showed a very low percentage of semi volatiles, and only very few fluorinated compounds were identified in that group. There are indeed expected emissions for the MCNM-based coating produced by incineration plants. Fig. 3b shows the probability that the innovative coating material is better or equal than the benchmark for each life cycle stage. This probability is 100% for the first four life cycle stages, while it is quite low (25%) for the end-of life stage. These results clearly demonstrate that the PFAS-free anti-sticking coating is superior to the more conventional Teflon application and therefore it is worthy to continue with its development and possible large-scale production.

The percentage of positive contributions, as previously reported for the life cycle stages, was also estimated for economic, environmental and social sustainability, safety and functionality (cf. Fig. 4). Specifically, Fig. 4a shows that the MCNM-based coating performs better in all these aspects except for functionality, for which the two alternatives score the same. This demonstrates that the novel coating is competitive with respect to Teflon because it is safer and more sustainable without compromising functionality. This conclusion is confirmed in Fig. 5a, where all positive contributions related to the two compared alternatives are integrated. Fig. 5a demonstrates that the innovative material has a higher percentage of positive contributions than the benchmark, while Fig. 5b shows that the probability that the innovative material is better or equal than the benchmark is 100%.

Fig. 6a shows that the innovative packaging performs better when considering the overall percentage of positive contributions than the LDPE for three out of the five assessed life cycle stages. In fact, the Raw materials and resources stage is the only one in which the innovative material has fewer positive contributions than the benchmark, and for the End-of-Life treatment stage the design alternatives score the same. Fig. 6b shows the probability that the innovative coating material is better or equal than the benchmark for each life cycle stage. This probability is 100% for four life cycle stages, while it is quite low (28%) for the End-of-Life stage. These results demonstrate that the innovative material is superior to the more conventional polymer packaging application and therefore it is worthy to continue with its development and possible large-scale production.

The percentage of positive contributions, as previously reported for the life cycle stages, was also estimated for economic, environmental and social sustainability, safety and functionality (cf. Fig. 7). Specifically, Fig. 7a shows that the MCNM-based coating performs better in all these aspects except for Economic sustainability, for which the two alternatives score the same. For social sustainability and safety aspects the related uncertainty is quite hight. Fig. 7b shows the probability that the innovative coating material is better or equal than the benchmark for each life cycle stage. This probability is practically 100% for all the LCS. This conclusion is confirmed in Fig. 8a, where all positive contributions related to the two compared alternatives are integrated. Fig. 8a demonstrates that the innovative material has a higher percentage of positive contributions than the benchmark, while Fig. 8b shows that the probability that the innovative material is better or equal than the benchmark is 100%.

5. Conclusions

This manuscript presents a structured approach to support SSbD decision making for advanced materials. The approach consists of three tiers: screening-level qualitative (Tier 1), semi-quantitative (Tier 2) and quantitative (Tier 3). Tier 1, which is the prime focus of this paper, is a self-assessment methodology that enables industries, especially SMEs to evaluate the safety, functionality and sustainability in the early stages of designing advanced materials/products. This is a lifecycle thinking approach: questions are divided according to the life cycle stages of the assessed materials/products and cover the environmental, social and economic dimensions of sustainability. Finally, to support SMEs in the comparison of possible design alternatives, the proposed approach has been implemented in a digital tool which facilitates comparison of alternatives and produces graphical charts of the results. Concerns identified through the questionnaire can be addressed by the industries early and at lower cost, which can have a substantial impact on their capacity to innovate. The questionnaire is helpful for the overall SSbD approach as it supports identification of hotspots of safety and sustainability concerns, and therefore guides the industries in the planning of further assessments in the subsequent Tiers. Moreover, the questionnaire can be applied to identify potential safety and sustainability issues, information gaps, concerns and regulatory needs.

The results of applying the approach in the Laurentia case study have shown that the novel PFAS-free coating has more positive contribution to sustainability compared to its conventional counterpart (Teflon) in terms of both safety and sustainability and the two alternatives are approximately equal in terms of functionality. Such results were obtained for all the assessed life cycle stages except for End of Life. This has identified a potential hotspot that needs to be further investigated in Tiers 2 and 3. Nevertheless the results have shown that the innovative coating has higher probability to be safer and more sustainable than the benchmark, which has encouraged the company Laurentia to invest into its further development, testing and possible large-scale manufacturing. Concerning the Encapsulae case study, the results have shown that the novel active food packaging has more positive contribution to sustainability compared to its conventional counterpart (LDPE) in terms of both safety and sustainability and the two alternatives are approximately equal in terms of economic sustainability. Such results were obtained for all the assessed life cycle stages except for Raw materials and resources. This highlights the necessity to further investigate the identified potential hotspot in Tiers 2 and 3. Nevertheless, the results have shown that the innovative food packaging has higher probability to be safer and more sustainable than the benchmark, which has encouraged Encapsulae company to invest into its further development, testing and possible large-scale manufacturing. Furthermore, both companies have identified areas where there is insufficient information, leading to uncertainty in the questionnaire. These gaps in information enable companies to determine which information they need to collect. Such information will be useful not only for the immediate tier but also for the ones that follow.

Declaration of competing interest

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

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cesys.2023.100132.

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