Accepted Manuscript

Submission Date: 2024-09-16
Accepted Date: 2024-12-05
Accepted Manuscript online: 2024-12-09

Sustainability & Circularity NOW

A Conceptual Framework for Safe-and-Sustainable-by-Design to Support Sustainable Business Model Innovation and New Product Development

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DOI: 10.1055/a-2498-8902

Please cite this article as: Stoycheva S, Peijnenburg W, Salieri B et al. A Conceptual Framework for Safe-and-Sustainable-by-Design to Support Sustainable Business Model Innovation and New Product Development. Sustainability & Circularity NOW 2024. doi: 10.1055/a-2498-8902

Conflict of Interest: The authors declare that they have no conflict of interest.

This study was supported by Horizon 2020 Framework Programme (http://dx.doi.org/10.13039/100010661), 952924, HORIZON EUROPE Digital, Industry and Space (http://dx.doi.org/10.13039/100018699), 10113732

Abstract:
In order to reach a sustainable future and meet the UN's Sustainable Development Goals (UN SDGs), business model innovation (BMI) needs to explore theoretical and practical intersections of the traditional innovation management (IM) and new product development (NPD) processes with sustainability considerations. New environmental and health policy ambitions such as those presented in the European Green Deal and the EU Chemicals Strategy for Sustainability (CSS) challenge traditional IM theories on BMI and NPD processes. The Safe-and-Sustainable-by-Design (SSbD) concept is a central element of the CSS and demands a novel approach that integrates innovation with safety, sustainability and circularity of materials, products and processes without compromising their functionality or their technical and/or commercial viability. Importantly, adopting such a concept can prevent regrettable substitutions, future liability and brand image issues for companies. To achieve this, companies must design products with minimal environmental impact, adopt circular economy principles, and ensure social responsibility throughout the value chain, whilst economic viable. By doing so, companies contribute to economic, environmental, and social sustainability. In this perspective, a conceptual framework is proposed on how to achieve sustainable BMI and NPD by integrating traditional IM tools with SSbD using life cycle thinking principles considering external and internal drivers.

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A Conceptual Framework for Safe-and-Sustainable-by-Design to Support Sustainable Business Model Innovation and New Product Development

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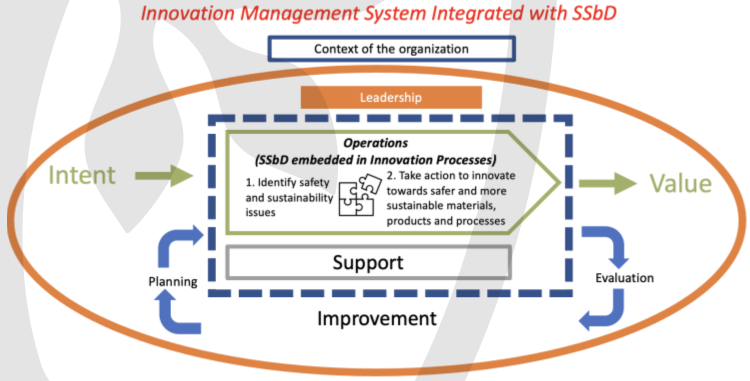
SIGNIFICANCE

- Business model innovation (BMI) and new product development (NPD) process need a sound framework for successful integration of safety and sustainability considerations in order to foster sustainable innovations.
- Safe-and-Sustainable-by-Design (SSbD) is central to meeting policy ambitions and could be integrated with traditional IM tools to support sustainable BMI.
- A conceptual framework is proposed to achieve sustainable BMI and NPD by integrating traditional IM tools with SSbD using life cycle thinking (LCT) principles.

SSbD and LCT should be embedded in the new certified training for professional designation for IM.

Innovation Management System Integrated with SSbD



Keywords
product innovation, new product development, SSbD, chemicals strategy for sustainability, future-proof innovation management system, sustainable business model innovation

submitted
accepted after revision
accepted manuscript online
published online

Bibliography
Sus. Circ. NOW 2023; x: SCNOW-0000X

DOI 10.1055/XXXXXXX
eISSN 0303-4259

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Additional material is available at https://doi.org/10.1055/SNOW-0000X.

ABSTRACT

In order to reach a sustainable future and meet the UN's Sustainable Development Goals (UN SDGs), business model innovation (BMI) needs to explore theoretical and practical intersections of the traditional innovation management (IM) and new product development (NPD) processes with sustainability considerations. New environmental and health policy ambitions such as those presented in the European Green Deal and the EU Chemicals Strategy for Sustainability (CSS) challenge traditional IM theories on BMI and NPD processes. The Safe-and-Sustainable-by-Design (SSbD) concept is a central element of the CSS and demands a novel approach that integrates innovation with safety and sustainability (including circularity) of materials, products and processes without compromising their functionality and/or commercial viability. Importantly, adopting such a concept can also prevent regrettable substitutions, future liability and brand image issues for companies. To achieve this, companies must design products with minimal environmental impact, adopt circular economy principles, and ensure social responsibility throughout the value chain, whilst maintaining economic viability. By doing so, companies contribute to environmental, social and economic sustainability. In this perspective, a conceptual framework is proposed on how to achieve sustainable BMI and NPD by integrating traditional IM tools with SSbD using life cycle thinking principles while considering external (changing legislation, new business standard requirements, competitive environments, technological developments, societal views) and internal drivers (company specific targets, company culture, corporate strategy, management capabilities). SSbD and life cycle thinking should be embedded in newly developed training for innovation management professional designation. This is because innovation managers can play a key role in bringing this transition into practice.

Introduction

Business model innovation (BMI) has become a well-established phenomenon in management and organization theory, and a central topic for debate in the innovation management (IM) field. But at the same time theoretical and practical explorations of the intersections between BMI, the new product development process (NPD) and sustainability remain somehow overlooked [1-3]. This is important given that NPD is the backbone of innovation, one of the major concerns of our modern society, and a key driver to achieving sustainable development.

BMI represents a highly relevant concept which is described in the literature in several ways: 1) a process by which management actively innovates the business model (BM) to disrupt market conditions [4]; 2) the discovery of a fundamentally different business model in an existing business [5]; 3) initiatives to create novel value by challenging existing industry-specific business models, roles and relations in certain geographical market areas [6]; 4) to search for new logics of the firm and new ways to create and capture value for its stakeholders [7], or 5) as a reconfiguration of the BM's elements, of the firm's activities or of the value proposition [5, 8-9].

In summary, the BMI perspective is seen as a holistic organizational innovation approach that helps to keep the big picture in mind instead of focusing only on specific innovation topics described by traditional IM [10]. Not surprisingly, the BMI construct has been intensively explored empirically within the IM research but predominantly from a strategy perspective [11-12], starting various lines of research looking at the antecedents, moderators and mediators, and consequences of innovating BMs [13].

Drivers for business model adaptation

Research has been focused on identifying drivers of business model adaptation which include pressure from external stakeholders [14-15], regulatory forces, changes in competitive environment [16], opportunities arising from new information and communication technologies [17-19], and changes in business environment [9]. Internal factors triggering BMI amongst others include organizational [20], and management capabilities [21], organizational culture [22], and changes in a firm's strategy [23] among others.

Performance implications, process and facilitators for business model adaptation

In addition to research on drivers there are three other partly overlapping research streams: performance implications [24-25], process [26-29] and facilitators of BM adaptation [4, 30-37]. Overall, BMI can be driven by internal and external factors [3]. The motivation for BMI is to shape markets or industries by means of creating disruptive innovations [5, 38] and not just aligning and adapting for strategic [39] or organizational [40] reasons.

Integrating sustainability to the process of NPD

Another central concept in IM looks at the process of NPD, which is based on the integration of multi-disciplinary knowledge (scientific, technological and market knowledge) resulting in a recognizably different product [41]. Looking at the knowledge base around sustainable NPD, prior research indicates that integrating sustainability considerations in the NPD process can be complex, risky, costly and time consuming [42-43].

Studies consistently indicate that incorporating sustainability in the NPD at an operational level should adopt a lifecycle thinking (LCT) approach [44] and cover environmental, social and economic impact assessments [44-46]. However, practical frameworks for this integration remain limited [43, 47-52]. Generally, organization and management literature offer sound models for IM such as the Cooper Stage Gate model [53-56] and the Funnel model [41]. These models contribute significantly to the field of NPD, but usually begin just after the point in the process where the idea has already been generated [57]. This "Fuzzy Front End" of NPD is often overlooked and is the focus point of this perspective [57]. In addition, there is a lack of in-depth exploratory studies explaining the sustainable NPD process in practical terms.

Finding strategies to link sustainability with business model innovation and NPD

The disconnect in the general organization and management literature between BMI, the NPD process and the sustainability of the firm can be viewed as problematic for several reasons. Therefore, the motivation of this study is both theoretical and practical and tackles timely real-world problems for industry and policy making.

First, from a management and practitioner's perspective, the design of innovative and sustainable BMs is crucial for commercializing novel ideas, technologies, and products [58-59]. Therefore, sound *theory* is needed to address the dynamic links between BMI, NPD and product sustainability.

Second, in the wake of an era where sustainability is at the forefront of *policy making* that advocates proactive, sustainable by design approaches and solutions, IM literature seems to fail to address the above-mentioned gaps. In the political arena, policy ambitions such the European Green Deal (EGD) triggered the EU Chemicals Strategy for Sustainability (CSS) [60] (EC, 2020) to encourage and steer the chemical industry towards a long-term green transition. This transition includes the development of safer and more sustainable chemicals, materials, products, processes and value chains [60-61][1]. As a result, *companies* and value chains are challenged to develop and apply safe and sustainable innovations in a LCT approach. LCT aims to address human and environmental impacts of chemicals, materials and products throughout their life cycles in an integrated way to avoid unintended consequences [62]. This ensures that the safety, economic, environmental, and social impacts are favorable and prevents adverse issues arising after market entry [63]. A multistakeholder and multidimensional approach along the entire value chain and throughout the life cycle is needed. This approach should involve all stakeholders to improve the support towards sustainable innovation [64], thus enabling the creation of innovative and sustainable ideas and integration of external knowledge to drive innovation, and balancing between functionality, safety and sustainability. The latter includes economic sustainability, circularity, and social and environmental

[1] We consider "safety" as an integral part of "sustainability". For the sake of aligning our vocabulary with the well-established SSbD trend, we use the term "safety and sustainability" in its meaning as "safety and other sustainability dimensions" (e.g. environmental, economic and social dimensions).

impacts.

Safe-and-Sustainable-by-Design and life cycle thinking principles as a strategy to achieve sustainable BMI and NPD

The Safe-and-Sustainable-by-Design (SSbD) concept is a central element of the CSS and demands the consideration of safety, sustainability and circularity of materials, products and processes without compromising their functionality and/or commercial viability [60]. SSbD aims at integrating safety and sustainability in the NPD process. Importantly, adopting such an approach can minimise the chance of regrettable substitutions (when one chemical is banned, only to be replaced with another chemical just as harmful, or potentially worse), future liability and brand image issues for companies. Safety and other sustainability dimensions need to be accounted for in all life cycle phases of chemicals, materials, products and processes in the innovation management system. Such a complex transformation goes far beyond just a single NPD process, and it is rather a case of sustainable BMI.

Sustainable BMI can be defined as a change in how a firm operates to create positive impacts or reduce negative consequences for the environment and society [65]. Whilst there is a broad consensus about the importance of sustainability for firms, research on the transformation towards sustainable BM remain rare [66, 67]. Indeed, prior research on the topic offers various reviews [68, 69, 70, 71], nevertheless the dynamics of implementing sustainable BMI remain relatively underexplored.
Furthermore, organization and management literature exploring the concept of SSbD for BMI is virtually absent.
It is therefore clear that a framework that explains how SSbD can be applied to the NPD processes is needed to transform the organizations' BMI towards safe, sustainable and circular products, processes and value chains. To address this conceptual gap, we investigate the following research question: *What are the forces, rules and conditions for a successful integration of safety and sustainability considerations in the BMI and NPD process?*

The broad objectives of this research are therefore:
1) to identify the dynamics for integrating sustainability with traditional IM systems and understand the forces that affect its realization, and
2) to develop a novel conceptual framework with guidance on how to integrate the SSbD with traditional IM tools to achieve sustainable products.

Multicomponent Nanomaterials (MCNMs) as a case study for the development of a conceptual framework how SSbD can be applied to support sustainable BMI and NPD

To achieve these objectives, this paper is informed by a combination of an exploratory [72] case study research spanning for an 18-month period in an SME manufacturing company producing novel advanced multicomponent nanomaterials (MCNMs) and an evidence-based literature review. The case study has been specifically chosen for several reasons.

First, the case of MCNMs is particularly interesting from a safety and sustainability assessment point of view. Despite being a key enabling cutting-edge technology, currently one of the greatest challenges of nanomaterial (NM) safety assessment is the rapid and diverse development of emerging manufactured NMs that consist of multiple conjugated components, such as in the case of MCNMs [72-76]. Due to their wide-ranging complexity (e.g. linkage of several NM types and forms, and/or NM-chemical combinations) an improved understanding is needed of how these components interact with each other, with other NMs and/or chemicals possibly leading to mixture toxicity, since unknown interactions may result in synergism, potentiation or antagonism of hazards.

It is also important to establish how the identities of the MCNMs and the products incorporating them change throughout their full lifecycle, spanning release, weathering and aging at different stages from manufacturing, to use and end of life [77-79]. Challenges of the sustainability assessment of MCNMs are similar to those sustainability challenges for chemicals. The ambition is to minimize consumption of raw materials and resources (water, solvents, land and energy consumption), minimize waste, and minimize the overall environmental footprint during design, manufacturing, production, transport, use and end-of-life [80]. It is also important to improve social benefits and optimizing economic feasibility, viability, and value [81-83].

This case study in Technology Readiness Level (TRL) 3/4 was a good methodological fit [84] to answer our research question; first deep dive into the challenges of applying SSbD to MCNM innovation and then extracting lessons learned to better link BMI, NPD, and IM with SSbD. In addition, it offered the research group unique access to follow a real innovation sustainability-driven process. It was considered theoretically fit to be able to adequately explain what has not been addressed by existing theory [85].

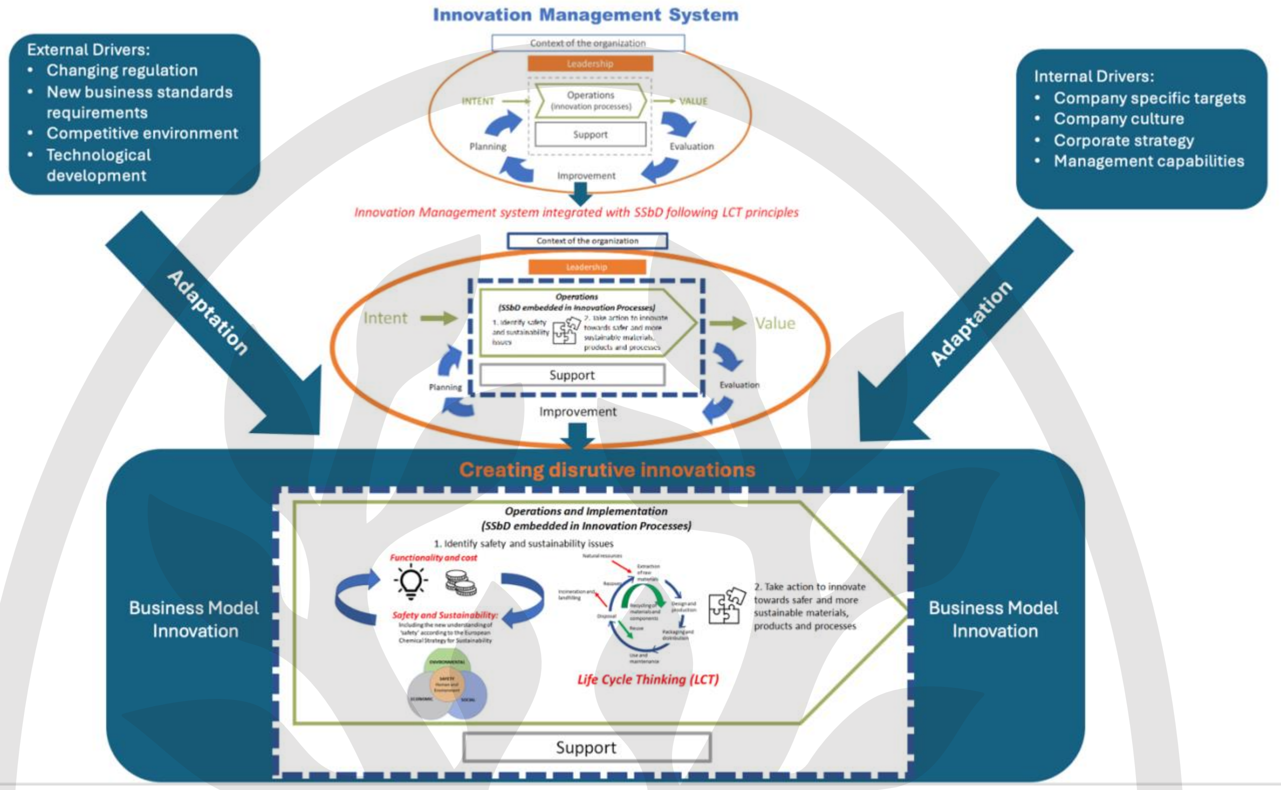
For our data collection, analysis and interpretation we used established best practices for data triangulation [72], and a grounded theory approach to offer an in-depth investigation of the sustainability-IM dynamics [86]. For the literature review, we followed the best practices for conducting systemic, evidence-based literature reviews from organization and management research (see Methods section).

This work makes contributions to various fields. At the practical level, it fills an important knowledge gap by providing a sound framework to support sustainable innovations. At the methodological level, it advances technical, environmental and organization and management sciences by bridging IM with safety and sustainability theories and practice through an exploratory case study of MCNMs. At the policy level, it contributes knowledge generation in support of the transition to a more sustainable future by providing a science-based conceptual framework that incorporates LCT and SSbD. In what follows, we proceed by giving an explanation of the background and motivation for the study and review ongoing debates in the sustainability and BMI literature exploring different theoretical positions that can shed light on the inner workings of these dynamics. Then we outline the methodology and present the results of the study. On this basis, we develop a conceptual theoretical framework explaining the relationships and mechanisms underpinning the integration of SSbD and IM practices. We then conclude by discussing the implications and limitations of the study and offering avenues for future research.

Results

A grounded model explaining the dynamics of sustainability-IMSs integration

Figure 1: A conceptual framework of sustainable business model innovation: the rules and guiding principles for successful integration of IM with SSbD following LCT principles



Although the innovation process usually follows a standard routine (following an IMS), it is characterized by constant changes, which are an attempt to accommodate different internal and external needs (i.e. changing regulatory demands, new business standards, changes in the competitive environment and technology development, etc. As the model (Figure 1) illustrates, there are various drivers, which affect organizations' innovation process and thus require a BM adaptation. Those stem from diverse pressures from the organizational field), which shape the formulation of IM changes. However, those pressures are translated into new business practices by passing through the prism of the company's identity, culture and capabilities (internal drivers). The main mechanism through which these changes are realized is BM adaptation. Once a disruptive element (such as incorporating SSbD which requires a thorough adjustment of the internal workings of the organization) is included in the IMS, a new BMI emerges. Our findings reveal some interesting observations, which both confirm and extend our current knowledge in those streams of research. Figure 1 represents the model developed based on our observations and confirmed by knowledge from existing literature.

The coherent, meaningful, and practical integration of an IMS with SSbD principles needs to be finely tuned in order to balance innovation with the criteria and tools from SSbD. As a foundation of our framework, we use the ISO 56002 standard for IMS [87]. The standard identifies seven key elements and eight principles that can be used to describe the IMS of an organization and its capabilities [88].

Following the ISO Standard, we developed a canvas (Table 1) which illustrates the rules and guiding principles for successful integration of IMS with SSbD following LCT principles. It includes the evidence-based literature review of 'by-design' principles and guidance from JRC reports [81-83, 89] and from the NanoReg2 EU-funded Project [90-91]. In addition, 'by-design' goals and strategies for safety and design criteria and guidance (possible 'by-design' actions) for sustainability are outlined for the development of the conceptual framework.

Traditionally, an IMS includes 7 key elements: Context (realization of value), Leadership (future-focused leaders), Planning (strategic direction), Support (culture), Operations (exploiting insights), Evaluation (managing uncertainty) and Improvements (adaptability & systems approach) [87]. In our conceptual framework (Table 1), the key elements of the SSbD IMS feature: 1) realization of value needs to include the changing policy landscape, for instance the EGD, CSS, the Critical Materials Act [92], Net Zero Industry Act and Circular Economy Action Plan, the Ecodesign for Sustainable Products Regulation (ESPR), where SSbD is central; 2) Future-focused leaders should have a vision and strategy aiming for safe and sustainable innovations; 3) The strategic direction of innovations should embed safety and sustainability criteria within the IMS; 4) Changing culture by facilitating an infrastructure consisting of a transdisciplinary dialogue between material scientists, engineers, (eco)toxicologists, economists, and sustainability and regulatory experts is vital to identify all safety and sustainability aspects and embed them efficiently within the innovation process, as well as bringing the value chain actors together; 5) Systemically building knowledge by applying safety and sustainability concepts during the innovation process; 6) Managing/reducing uncertainty by setting up a monitoring schemes to assess the criteria and performance indicators for the implementation of SSbD and LCT principles; 7) The integration of

SSbD into the IMS will ensure adaptions to improve or change functionality will not adversely impact upon safety and sustainability. Based on the evaluation, specific strategies and control measures should be proposed to guarantee safer and more sustainable processes throughout the product life cycle. IM is based on a systems approach, with interrelated and interacting elements, and regular performance evaluation and improvements of the system are needed (Table 1).

SSbD strategies have been developed and illustrated in Table 1 which are in line with the considerations of the first national Chemical Leasing initiative driven by the German Federal Environment Agency in 2009, and include: 1) Reduction of adverse impacts for environment, health, energy and resource consumption caused by chemicals and their application and production processes; 2) No substitution of chemicals by substances with a higher risk; 3) Improved handling and storage of chemicals to prevent and minimize risks; 4) Generation of economic and social benefits; and 5) Monitoring of the improvements [93].

Also, the three main safe-by-design pillars [91] (Table 1) have been adopted to be integrated into an IMS. The safety and sustainability assessment follows a stepwise approach according to the following steps: i) hazard assessment of chemicals and materials (including human health, environmental and physical hazards), ii) Human health and safety aspects in the chemical/material production and processing phase (occupational safety and health aspects including acute and chronic human health hazards, physical properties, hazards from release behavior, and process-related hazards), and iii) human health and environmental aspects in the final application phase [81]. Step four (iv) is environmental sustainability and aims to maintain and preserve the environment and natural resources, without hampering economic development, by minimizing the environmental footprint, promoting circularity, and minimizing the waste and emission generated at each life cycle stage of the new material. Social sustainability (step v) is addressed by considering health and safety aspects related to the manufacturing, use, and end of life stage of the product. Also, social criteria such as support to basic human rights, transparency and responsible communication, consumer product experience, are included. Economic sustainability ensures economic stability and that the material, chemical, product and processes are economical and efficient.

MCNM case study major findings

The project managers in the SME addressed the SSbD challenges by developing a multi-disciplinary innovation ecosystem and bringing together the different expertises in material science, human and environmental toxicology, sustainability (environmental, social, economic, recycling) and regulatory. This was possible because the innovation managers of the SME were part of a European Project. In general, SME innovation managers do not have the expertise in-house, yet they can apply alternative strategies such as taking part in external partnerships, creating networks with academia or reaching out to consultants to have access to the necessary expertise. There were several SSbD strategies employed. For the safety aspect, strategies included: substitution of hazardous substances with MCNMs, optimization of powder handling to reduce worker exposure, replacing solvents in process for safer process safety, using liquid versus air suspension and reducing the release/migration. For the sustainability aspect, strategies included: replacing critical raw materials with MCNMs, reducing water consumption, reusing material lost during production, reducing energy use in the production process, recycling and reusing the solvents lost in the process by distillation, reducing CO2 emissions, improving recyclability of materials, and decreasing time and temperature in the process. The results of two real industrial case studies using the framework from the project have been recently published [94], 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 [94]. In this context, '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, versatility and reliability have been used to measure functionality.

Strategies for dealing with data scarcity early in innovation

In the case study of MCNM, a qualitative, screening approach was used to identify potential safety and sustainability issues at an early Research and Development (R&D) phase [94]. This type of screening approach revealed information gaps and raised awareness of potential safety and sustainability concerns, which in turn triggered the need for action. For 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 the entire life cycle; mainly with *in silico* methods (read-across) and expertises from the multi-disciplinary team. Other aspects such as 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, bio-accumulating substances from the product, and the transformations of any released MCNM were also assessed along the life cycle were also considered. For the environmental sustainability dimension, aspects considered included 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. For the social sustainability dimension, aspects considered included: 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

Table 1: Conceptual framework integrating IM with SSbD following LCT principles: Overview of ‘by-design’ goals and strategies for safety and design criteria and guidance (possible ‘by-design’ actions) for sustainability from JRC reports [81-83, 89] and from NanoReg2[90-91].

Integration of IM with SSbD following LCT principles

IM element: CONTEXT

- Realization of value by applying SSbD, circular and regenerative strategies. See recent screening level approach to support companies in making safe and sustainable by design decisions at the early stages of innovation [94].
- Better dealing with the ‘Fuzzy Front End’ of innovation funnel [57] while keeping up with policy landscape is changing through the EGD, CSS, Critical Raw Materials Act, Zero Pollution Industry Act, and Circular Economy Action Plan where SSbD is central.

Discovery	***Definition***	***Design***	***Development***	***Delivery***
What is the opportunity that we might want to pursue?	What detailed needs must we satisfy?	How can we satisfy those needs: that is, can we come up with better features and solutions than those that already exist?	Which of these prospective features or solutions are actually worth investing in?	The final shakedown process: Can we reliably produce it, sell it, maintain it, and make money doing it? (questions adapted from Katz [57]).
Who is the customer that we want to target?	How should we measure how well we’re satisfying them: that is, to what specifications should we design?	How do we describe these features and solutions to our customers such that they will find them compelling and believable?	Which should we actually include in the final product?	
What are their major problems, from a high-level perspective, in achieving the task they have chosen to undertake?			If we do, how much will people be willing to pay for them?	

IM element: LEADERSHIP

- Vision and strategy should aim for safe and sustainable innovations. A “do nothing strategy” is not sufficient. Companies must adopt circular, SSbD, and regenerative elements in their business models, start pilot initiatives, and build a transition strategy [94].
- SSbD supportive business models [102-106].
- Regenerative business models are based on the principles of sustainability, a circular economy, and biomimicry:
    - Sustainability: Regenerative businesses prioritize the health of the environment, and the well-being of the people involved in their operations. They aim to create a sustainable future by minimizing their negative impact on the environment and actively restoring and regenerating natural systems.
    - Circular economy: Regenerative businesses adopt circular economy principles by designing products and systems that are restorative and regenerative. This includes:
        - Circular inputs – using renewable, recycled, or highly recyclable inputs in production processes – enabling partial or total elimination of waste and pollution, while waste becomes an asset;
        - Sharing economy concept - maximizing how idle assets are used across a community while providing customers with affordable and convenient access to products and services);
        - Product as service – where the customer purchases a service for a limited time while the provider maintains ownership of the product and remains incentivized for the product’s ongoing maintenance, durability, upgrade, and treatment at the end of its use;
        - Product use extension – designing products for repairability, upgradability, reusability, ease of disassembly, reconditioning, and recyclability of all components;
        - Resource recovery – focusing on the end stages of the usage cycle, namely the recovery of embedded materials, energy, and resources from products at the end of use that is no longer functional in their current application [94].
    - Biomimicry: Regenerative businesses take inspiration from nature and adopt biomimicry principles in their operations. They aim to create systems that mimic natural processes and functions, such as closed-loop systems and regenerative agriculture [97].

IM element: PLANNING Embed safety and sustainability criteria within the IM system. IM element: OPERATIONS Apply safety and sustainability concepts during the	**Safety**	**Other Sustainability Dimensions**	
	Goal/Strategy	**Goal**	**Strategies**
	Goal: Safe(r) material Strategy: Design-out hazardous properties without affecting functionalities	Goal: *Material efficiency* Description: Incorporating all the chemicals or materials used in a process in the final product or fully recovering them inside the process, thereby reducing the	• Maximize yield during reaction to reduce chemical or material consumption. • Recover more unreacted chemicals or materials. • Select materials and processes that produce less waste. • Identify the occurrence of the use of critical raw materials, in order to minimize or

innovation process.		amounts of raw materials needed and generating less waste.	substitute them.
	Goal: Safe(r) process Strategy: Minimizing release and potential exposure scenarios (occupational and environment).	Goal: *Minimize the use of hazardous chemicals or materials* Description: Preserving the functionality of products while reducing or completely avoiding the use of hazardous chemicals or materials where possible. Using the best technology to avoid exposure at all stages of the life cycle of a chemical or material.	• Reduce and/or eliminate hazardous chemicals or materials in production processes. • Redesign production processes to minimize the use of hazardous chemicals/materials. • Eliminate hazardous chemicals or materials in final products.
	Goal: Safe(r) use and end-of-life Strategy: Minimizing release and potential exposure scenarios (user and environment).	Goal: *Design for energy efficiency* Description: Minimizing the energy used to produce and use a chemical or material in the production process and/or in the supply chain.	Select or develop (production) processes that: • involve alternative and less energy-intensive production/separation techniques. • maximize energy re-use (e.g. integration of heat networks and cogeneration) • have fewer production steps. • use catalysts, including enzymes. • reduce inefficiencies and exploit available residual energy in the process or select lower temperature reaction pathways
		Goal: *Use renewable sources* Description: Conserving resources, by means of resource-closed loops or by using renewable material and energy sources.	Promote the use of feedstocks that: • are renewable. • are circular. • do not create land competition. • do not negatively affect biodiversity or processes that: • use renewable energy resources with low-carbon emissions and without adverse effects on biodiversity
		Goal: *Prevent and avoid hazardous emissions* Description: Applying technologies to minimize or avoid hazardous emissions or the release of pollutants into the environment.	Select materials or processes that: • minimize the generation of hazardous waste and hazardous by-products. • minimize the generation of emissions (e.g. volatile organic compounds, total organic carbon, acidifying and eutrophication pollutants, and heavy metals).
		Goal: *Design for End of Life* Description: Design chemicals and materials so that, once they have served their purpose, they break down into chemicals that do not pose any risk to the environment or to humans. Design chemicals and materials in a way that makes them fit for re-use, waste collection, sorting and recycling.	Avoid using chemicals or materials that impede end-of-life processes such as recycling. Select materials that are: • more durable (longer life and less maintenance). • easy to separate and sort. • valuable even after being used (commercial afterlife). • fully biodegradable for uses that unavoidably lead to release into the environment or wastewater.
		Goal: *Consider the whole life*	Consider:

		cycle Description: Applying the design criteria to the entire life cycle, from the raw materials supply chain to the final product's end of life.	• using reusable packaging for the chemical or material being assessed and for chemicals or materials in its supply chain. • energy-efficient logistics (e.g., reducing transported quantities, changing the means of transport) • reducing transport distances in the supply chain
		Goal: *Design to minimizing negative and foster positive social impacts.*	• Minimize occupational and consumer health risks: support health & safety of local community's living conditions, safety management a work, management of worker's individual health, product safety, impact on consumer health. • Human rights: Support basic rights & needs including fair wages, appropriate working hours, no forced labor, human trafficking and slavery, no discrimination, social/employer security and benefits, access to basic needs, respect for human rights and dignity. • Social benefit: Contribute to economic and technology development via fostering education, job creation, joint research. • Support skills, knowledge and employability, promotion of skills and knowledge for local community and consumers. • Governance (value chain): promoting value chain with social responsibility
		Goal: *Design to optimize economic impacts*	• Use life cycle costing (LCC) to assess and optimize total cost over the life cycles the product including externality costs (e.g. the costs associated with environmental emissions, worker safety, and health protection, and land eco-remediation • Functionality (optimize product performance) • Optimize product cost (purchase and production cost) • Optimize profitability (added value, net present value, financial profit and payback period)
IM element: EVALUATION • Measure progress. Companies should measure their progress towards their circular, SSbD and regenerative goals and track the impact of their efforts. • Set up a monitoring scheme to assess the process of innovating with SSbD and LCT principles.			
IM Element: IMPROVEMENT • Identify areas for improvement and adjustments.			
System Approach • Embed SSbD in the system approach through iterative cycles of evaluation and improvement.			

of Life treatment options. For the economic sustainability dimension, aspects considered included 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. This screening approach is in line with the scoping analysis in the EC JRC SSbD methodological guidance [83] where the information needed to define the SSbD system is assessed through the engagement with the SSbD system partners for the application of the framework, and where the nature and purpose/objective of the (re)design of the SSbD system is identified. It needs to be kept in mind that this in an iterative process.

The strategies applied for dealing with data scarcity in the MCNMs case study were to first rely on the extensive knowledge of the multi-disciplinary team, followed by *in silico* approaches such as Quantitative-Structure-Activity-Relationships (QSARs), read-across and integrated approaches to testing and assessment (IATAs). Later in the innovation process, New Approach Methodologies (NAMs), including high throughput screening and *in vitro* assays are considered. For MCNMs, extra considerations are needed to account for a) the complexity of physical and chemical composition; b) the emerging properties driving the MCNM functionality; c) the potential for MCNM components to transform with different kinetics, leading to complex exposure scenarios; d) prioritisation of grouping decisions related to material properties (what they are), fate/toxicokinetics (where they go) and the hazard mechanisms (what they do). From a sustainability perspective, exante/prospective Life Cycle Assessment (LCAs) are used early in the innovation process, followed by full LCAs later in the innovation process.

Reflections

Having innovation managers identify the relevant safety and sustainability issues early in the innovation process increases the speed and likelihood to bring solutions to the market ('fail early, fail cheap' logic) and shape the successive trade-off decisions. Uptake of the framework can be accelerated by educating innovation managers and stimulating multi-disciplinary collaborations. The biggest advantage of this framework is that for the innovation manager the number of potential candidates is reduced with increasing TRL, leaving only a small number of promising candidates going into the scale-up phase. The SMEs from the project have extended the application of SSbD to other case studies by applying the lessons learned from this work. The biggest challenge is to have an assessment framework that is supported by data and tools to allow the identification of the non-viable options as quickly as possible within any innovation process.

Discussion

This perspective proposes a conceptual framework on how to integrate IM tools with SSbD using life cycle thinking principles considering external (changing regulation, new business standard requirements, competitive environment, technological developments, societal views) and internal drivers (company specific targets, company culture, corporate strategy, management capabilities) to achieve sustainable BMI and NPD. It attempted to answer some central yet uninvestigated topics in innovation management literature by offering unique multidisciplinary insights. Our work is directly relevant for both theory and practice as the design of innovative and sustainable BMs are crucial for commercializing novel ideas, technologies, and products. At the same time, our results are timely and relevant for the global policy agenda which seeks to operationalize SSbD/Design for sustainability efforts in order to contribute to achieving sustainable development.

SSbD following LCT principles aims to support companies and innovation managers to anticipate safety and sustainability impacts and to address these without compromising the functionality of the material, chemical, product and process. It supports decision making in each step of the innovation process and allows innovators, manufacturers, organizations, industry, companies, and policy makers to identify opportunities for improvements and consequently to pinpoint those life cycle segments with the most significant impact on safety and sustainability.

Our key technical result was the development of a canvas which illustrates the rules and guiding principles for successful integration SSbD following LCT principles in IMS. Our work reveals several insights on how this is done in practice and develops practical recommendations.

From a *context perspective*, SSbD has implications for management systems including assessing value chain safety and sustainability impacts in IM, in addition to external and internal issues and trends.

From a *leadership perspective*, senior management should adopt SSbD-supportive BMs and demonstrate leadership and commitment by establishing an innovation vision, strategy, and policy, including the necessary roles and responsibilities [64, 95-99]. In addition, SSbD and LCT should be part of the training of the new profession designation for IM to ensure managers are equipped with the right skills needed in innovation roles [100].

Lessons learned

A multi-disciplinary team is needed to facilitate and accelerate safe and sustainable innovations

From a management perspective, a transdisciplinary dialogue between material scientists, engineers, human and environmental toxicologists, and professionals and experts in sustainability, recycling and regulation, is needed to identify all safety and sustainability aspects, along each life cycle stage, while, at the same time, retaining product performance and economic efficiency. There are communication issues that need to be overcome to achieve a LCT approach and connect stakeholders in the lifecycle.

SSbD is only possible when clear and simple communication of data *on safety and other sustainability dimensions, both internally and externally, between different disciplines and stakeholders*

Any operational SSbD following LCT principles will require data relating to the different safety and sustainability dimensions early in the innovation process. The framework for SSbD criteria [81] outlines how to define the data needs for the safety and environmental dimensions of SSbD. Here, grouping and read-across framework [101] have been developed to support efficiency yet reliability of data assessment. Also, the eNanoMapper (https://www.enanomapper.net/) is a good example of generation of FAIR data and common reporting templates.

Different LCA tools require lots of data and expertise

For sustainability to be taken into consideration from an early stage of the innovation process, the use of sustainability assessment tools (i.e. Environmental-LCA (E-LCA), Social-LCA (S-LCA), Lifecycle Costing (LCC) should be applied to support the decision-making process. Indeed, these tools can be applied along the innovation process to compare alternative SSbD measures, to identified potential hotspots/red flags/issues (e.g. resource use during the production process), and hence identify measures to minimize the environmental footprint of a material [102]. E-LCA has been already applied in several sectors (chemical, food, energy, building etc.) and several studies have been published on nanotechnologies [103-104]. An E-LCA based approach offers the advantage of providing a broader view on the environmental performance (i.e. on climate change, resource use, ecosystems and biodiversity), allows to address potential impacts at each life cycle stage, and enables the investigation of different scenarios before a novel material or new technology is launched into the market. A recent screening level approach that supports companies in making safe and sustainable design decisions at the early stages of innovation has been published [94].

Including social and economic aspects in SSbD and IM is crucial

JRC reports [80-83, 88] provide guidance on economic and social impact of products. Social LCA has been developed with a list of relevant criteria and data needs. System boundaries need to be harmonized for economic and social LCA with the environmental LCA in their joint application [105]. Recently an easy-to-use, cost and time-efficient socio-economic analysis was developed to guide users through their SSbD decision making regarding newly developed advanced materials and nano-enabled products. The results of this initial screening can be further used for more detailed analysis in the later stages of product development by performing a full social life cycle assessment (S-LCA) [106].

Innovation managers need multidisciplinary training to apply SSbD

The profession designation for IM along with the development of a codified body of knowledge in IM (for instance, the ISO 56002 Guide Standard) is an opportunity to ensure managers are equipped with the right skills needed in innovation roles [100]. The IM profession designation should integrate SSbD and LCT in their curriculum to be able to support safe and sustainable product innovation. This multi-disciplinary team needs to be able to work effectively together to co-create SSbD strategies.

Summary of theoretical, managerial and policy implications

Scholars investigating (sustainable) BMI have largely focused their attention on developing lengthy descriptions of sustainable BMI mainly from a strategic point of view while little attention has been paid to "opening the black boxes" and engaging in a more exploratory focus. At a theoretical level, an important contribution of this study is the development of a grounded conceptual model that explains the mechanisms through which the innovative sustainability-IMS integration process is realized. We have identified various drivers, which affect organizations' innovation process and thus require a BM adaptation. These are driven by diverse external pressures from the organizational field (i.e. changing regulatory demands, new business standards, changes in the competitive environment and technology development, etc.) and internal (company centric) such as company identity, culture and capabilities. Whilst these changes impose BM adaptation, once a disruptive element (such as incorporating SSbD) is included in the IMS, a new BMI emerges.

At the *practical level*, it fills an important knowledge gap by providing a sound framework to support sustainable innovations (See discussion section for more detailed managerial implications).

At the *methodological level*, it advances technical, environmental and organization and management sciences by bridging IM with and safety and sustainability theories and practice exploring the unique case of MCNMs.

At the *policy level*, it contributes to the generation knowledge in support of the transition to a more sustainable future by providing a science-based conceptual framework that incorporates LC and SSbD thinking.

Limitations and future research

We acknowledge the limitations of our study. First, stemming from the exploratory focus of the research, our findings reveal interesting results about the realization of sustainable BMI following an "idealized" innovation process following ISO standard frameworks while in reality many innovations do not follow such a strict routine. In addition, informed by a single case this research is able to capture one side of the sustainability-innovation dynamics. A future line of research that can complement these findings could be a replication study or multi-case study approach to further confirm and enhance the suggested framework (to ensure the uptake and utilization of the proposed framework, it will be tested in the newly started Horizon Europe SUNRISE project (www.sunrise-horizon.eu). Specifically, we acknowledge that a more comprehensive investigation of other various disruptive elements (such as the SSbD concept) can change the BMI process. Second, our canvas represents an integration of evidence from various literature including frameworks that are currently being tested and further revised. Future research should focus on incorporating such revisions and operationally testing the framework. Although such research project may be difficult and timely to conduct due to problems of access, we foresee it as a promising research agenda, which can provide a more holistic view on how the business community experiences and implements innovative sustainability practices in their operations. Such a research agenda can make a significant contribution to organization and management theories by closing the gap between the world of practice and theory. A summary of future lines of research is provided in Table 2.

Table 2: Future lines of research.

Field	Future research lines/questions
Management and Organisation Science	• Replication or multi-case study approach to enhance and validate the developed framework • What other disruptive elements affect the dynamics and implementation of sustainable BMI?
Environmental and Material sciences	• Testing the framework in real industrial case studies

Conclusions

Driven by the need for BMI and NPD to explore intersections with sustainable IM, this perspective introduces SSbD as a tool for environmentally sustainable innovations. A conceptual framework is proposed on how to integrate IMS with SSbD using LCT principles, without compromising product functionality or their technical and/or commercial viability. Challenges and possibilities of integrating SSbD and LCT to IMS are discussed given that SSbD is a central component of the CSS. Transitioning to a 'by-design' thinking means adopting a new way of working by integrating safety and sustainability as early as possible in the innovation process. This new way of working can be put into practice by integrating SSbD to IMSs.

For practitioners, integration of SSbD following LCT principles to IM requires:

From an *operational view*, prioritizing 'by-design' thinking and integrating SSbD in IM practices. Supporting strategies include:

- Obtaining relevant data on safety and other sustainability dimensions at reasonable levels of resources;
- development and use of integrated safety and sustainability databases;
- better use of in silico approaches such as read-across;
- development of tools integrating and weighing safety and sustainability;
- further development of social and economic tools

From a *planning and operations perspective*, embedding and applying safety and sustainability criteria within the IMS as early as possible in the innovation process.

From a *management perspective*:

- An SSbD and LCT Management System is needed that not only steers innovation, but also aims towards a safe and sustainable innovations that supports the company's management portfolio by preventing regrettable substitutions, future liability and brand image issues for companies. Safety and sustainability need to be accounted for in all life cycle phases of chemicals, materials, products and processes in the IMS. The proposed conceptual framework shows how to integrate IM (particular planning and operations) to ensure that the design and development of chemicals, materials, products and processes are safer and more sustainable for humans and environment, and deliver the expected performance and value to stakeholders throughout the value chain;
- A reorganization of internal company infrastructure and process to facilitate a transdisciplinary dialogue between material scientists, engineers, human and environmental toxicologists, and professionals and experts in sustainability, recycling and regulation, is needed to identify all safety and sustainability aspects, along each life cycle stage, while, at the same time, retaining product performance and economic efficiency.

From a *planning perspective*, a quality control system related to the IM is needed along with the development of an SSbD monitoring system.

From an *education and training perspective*, the training of innovation managers to SSbD thinking is essential as the recent professional designation for IM is an opportunity to have greater influence in organizational strategy and bringing SSbD closer to practical applicability to meet policy ambitions and towards the development of a future-proof innovation system.

Methodology

Conceptual Background

This section explores the main discourse around sustainable BMI and introduces in detail the current SSbD knowledge base. This section also advocates the need for a sustainable NPD and BMI based on the presented SSbD case study that serves as a background to explain our resulting framework.

(Sustainable) business model innovation

A recent movement in literature is the emergence of sustainable BMI, which is described as a change in the way a firm operates to create positive impacts or to reduce negative consequences for the environment and the society [65]. Sustainable BMI is characterized by (1) the incorporation of sustainable principles or goals into the existing value proposition, (2) the extension of value creation concept from economic value to shared value [107], (3) the consideration of non-financial interests in the decision-making process and (4) managers who act as sustainability leaders to promote a new mindset within the whole organization [108]. A key activity of sustainable BMI is transforming a standard value proposition toward a more sustainable value proposition that allows value creation by considering the needs of customers, shareholders, suppliers, partners, community, society and environment [109].

Recently, a new framework was proposed to include value proposition, value creation delivery and value capture [100]. For the value proposition, a new sustainable value is needed that supports a renewed purpose arising from an authentic motivation and passion within the firm's organizational culture. Within the customer's sphere, there is a need to create value and the essential resources, activities and partnerships to deliver, including a guarantee for transparency and ethics [65]. It is important to note that there are four types of sustainable BMI: (1) sustainable start-ups creating a new organization with a sustainable BM; (2) sustainable BM transformation where the current BM is changed, resulting in a sustainable BM; (3) sustainable BM diversification where a sustainable BM is established without major changes in the existing BMs of the organization; and 4) sustainable BM acquisition where an additional, sustainable BM is identified, acquired, and integrated into the organization [14, 71]. Nine generic sustainable BM strategies (or 'archetypes') have been developed by Bocken et al. [69] and Ritala et al. [110]: (1) maximise material and energy efficiency; (2) closing resource loops; (3) substitute with renewables and natural processes; (4) deliver functionality rather than ownership; (5) adopt a stewardship role; (6) encourage sufficiency; (7) repurpose for society or the environment; (8) inclusive value creation; and (9) develop sustainable scale up solutions.

Even though there is progress in the direction of sustainable BMI, a validated measurement scale for sustainable BMI is not yet available [111]. A ten-item scale has been conceptualized under sustainable value proportion innovation, sustainable value creation and innovation delivery, and sustainable value capture innovation [111]. Considering the great interest towards sustainable BMI, it is clear that the field is in its infancy, and more research is needed in order to better understand this phenomenon.

In summary, whilst previous literature has defined well that sustainable BMI emerges as a complex multistakeholder transformation process which often involves incorporating heterogeneous metrics based on various stakeholders' needs [112], the dynamics and the internal workings of this process have been overlooked. Furthermore, Lozano [113] and Geissdoerfer et al. [71] identified a gap in the research around sustainable BMI design and implementation. Our work aims to answer this call and advance previous literature on this topic [i.e. 65] by offering a novel framework which explores the dynamics for integrating sustainability with traditional IM systems and explains the forces that affect its realization.

Policy landscape

In the policy arena, recent initiatives such as Design for Sustainability (D4S) [114] and the EC's publications on SSbD chemicals and materials [80-83, 88] provide knowledge in the field of SSbD. In particular SSbD forms a clear case for interlinking sustainable BMI, NPD and IM.

After the publication of the CSS, the EC's Joint Research Centre (JRC) has reviewed safety and sustainability dimensions, aspects, methods, indicators, and tools [89] and developed the SSbD framework [81]. The SSbD framework aims to i) steer the innovation process towards the green and sustainable industrial transition, ii) substitute or minimize the production and use of substances of concern, in line with, and beyond existing and upcoming regulatory obligations; and iii) minimize the impact on health, climate and the environment during sourcing, production, use and end-of-life of chemicals, materials and products. Successful implementation of SSbD will ensure the design and development of chemicals and materials that are safer and more sustainable for humans and environment and deliver the expected performance and value to stakeholders throughout the value chain, so determining the future of innovation. A JRC Technical Report on the first applications of the SSbD framework to case studies was published [82] along with methodological guidance [83]. After a testing period, SSbD criteria will be developed for the application and assessment of SSbD. Organizations such as the European Environment Agency, the Organisation for Economic Co-operation and Development Working Party on Manufactured Nanomaterials Safe(r) and Sustainable Innovation Approach (SSIA) Steering Group, the European Chemical Industry Council (Cefic), and the International Chemical Secretariat (ChemSec) are all contributing to bringing SSbD to practice [114-121].

The EC Recommendation [122] on establishing a European assessment framework for SSbD chemicals and materials describes key expected actions by industry including i) using the SSbD framework when developing chemicals and materials; ii) making available FAIR (findable, accessible, interoperable and reusable) data for safe and sustainable by design assessment, iii) supporting the improvement of assessment methods, models and tools, and iv) supporting the development of professional training and educational curricula on skills related to safety and sustainability of chemicals and materials.

Based on the performed analysis, key issues were identified that relate to bringing SSbD to practical applicability and integrating safety and sustainability into the innovation process and one solution identified to achieve this goal is to embed SSbD into IM systems (IMS) including BMI and NPD. While both theory and practice lack an in-depth clear explanation of how such integration should be realised, here we propose a conceptual framework on how to integrate IMSs with SSbD using life cycle thinking principles considering external (changing regulation, new business standard requirements, competitive environment, technological developments, societal views) and internal drivers (company specific targets, company culture, corporate strategy, management capabilities).

Our work bridges knowledge from several fields (environmental, material, management and organization sciences) thus providing a unique contribution to the various fields. It supports both policy and practice by providing a sound framework to support sustainable innovations and the transition to a more sustainable future. From a methodological perspective, it advances technical, environmental and organization and management literature by bridging IM with safety and sustainability theories and practice through an exploratory case study of MCNMs.

Detailed Methodology

This study incorporates a combination of varied methodological approaches employed by a multidisciplinary research team to convene into a single framework able to incorporate knowledge from environmental scientists, regulatory experts, social and sustainability scientists that can "speak" to various stakeholders. However, as our main target audience are innovation management scholars and practitioners, the research agenda was predominantly led by the best practices to conduct exploratory studies in management and organization fields. In specific, 1) we used a case study approach to explain theoretically the process of integrating sustainability with IMS and understand the forces that affect its realization, 2) at a technical level following the EC Recommendation [122], a literature review was done to support an evidence-based approach to create the building blocks of a novel conceptual framework, supported with guidance, that assists users to integrate SSbD with traditional IM tools to achieve environmentally sustainable innovations.

Case study

Research setting: This research was informed by the unique opportunity to explore the work of an SME aiming at creating a novel MCNM designed to be used for food applications. The company's intention is that it should outperform conventional materials with the same application from a safety and sustainability point of view whilst maintaining functionality. This was a collaborative work in the framework of an ongoing research and innovation project, H2020 SUNSHINE, and involved a participant observation period of nearly 18 months granting the opportunity to employ data collection methods commonly used for ethnographic research [123]. Methodologically, these conditions grant that the research relies on the logic of theoretical sampling falling under the condition of presenting an opportunity for an unusual research access [72]. Moreover, the situated analysis [124] adopted here provided a rich avenue to capture the micro-level dynamics of the sustainable BM implementation meta-routine [125], which gave insights not only from within but also across a number of routines constituting the meta-routine realization.

Data collection: This study employed data collection methods commonly used for ethnographic research [123], such as participant observation, formal in-depth semi-structured interviews and informal conversations. The data collection was complemented using additional secondary sources, such as the company publicly available data in the form of official documents available on the company website, press releases and news articles.

Data analysis: The data analysis was conducted in an iterative fashion consistent with an inductive, grounded theorizing approach [85, 126], that involved developing insights by analyzing the primary and secondary data, emerging observations, and existing literature in an iterative process [127]. The analysis followed the exemplar first- and second-order analysis approach [86], which involved i) extracting recurrent concepts and themes through *in-vivo* codes (i.e. assigning labels to a section of data, using a language taken from that section of the data) and descriptive coding (i.e. summarizing the basic topic of a passage of qualitative data) and grouping them into emergent categories (first-order analysis), followed by ii) moving the analysis to a more theoretical level aimed at extracting the explanatory dimensions from the emerging patterns of data via seeking for relationships between and among first-order findings to facilitate assembling them into higher-order themes (second-order analysis).

Literature review to support evidence-based approach

We followed the best practices for conducting systemic, evidence-based literature reviews [128] to obtain the building blocks for the development of the novel integrative framework. The main aspects of this approach, as summarized in [128] were: i) development of clear and precise aims and objectives; ii) pre-planned methods; iii) comprehensive search of all potentially relevant articles; iv) use of explicit, reproducible criteria in the selection of articles for review; v) an appraisal of the quality of the research and the strength of the findings; vi) synthesis of individual studies using an explicit analytic framework; vii) balanced, impartial and comprehensible presentation of the results. Following the method, a review protocol was designed to address the above stated question, containing specific rules for inclusion/exclusion criteria, a quality assessment tool (based on expert judgment) and a common data extraction format.

Firstly, an overview of different IMSs and SSbD approaches was made, including those developed in previous EU-funded projects and in the recent framework developed in the context of implementing the EC CSS [81-83, 89-91, 102-103, 117-119, 129-131]. An overview of regulatory and policy documents supporting some aspects of SSbD was made and presented in Supplemental Table 1. To support the application of SSbD with currently used International Organization for Standardization (ISO) standards, an overview of ISO documentary standards supportive of certain SSbD aspects (Supplemental Table 2) was made and the standards were classified according to the SSbD relevant elements contained therein as structure, process and content. In ISO terms, structure refers to the organizational elements that need to be in place to implement some aspects of SSbD (e.g. specific department or individual roles) including context and leadership. A "process" refers to the way to implement it (e.g. design or audits) including planning and support. Finally, "content" refers to criteria and other content related aspects (e.g. LCT) used to measure progress and improvement. It can be seen from Supplemental Table 2 that ISO standards offer most guidance on process aspects, followed by content and, finally, structure.

Secondly, an inventory of 'by-design' criteria and guidance from JRC reports [81-83, 89] and from the NanoReg2 EU Project [90-91] (Supplemental Table 3) was made. This was generated from an overview of information needs for assessing safety and sustainability. For this, a literature review was performed with the search terms 'safe-by-design'; 'SSbD'; 'safety tools'; 'sustainability tools'; 'safety and sustainability information needs and safe-by-design'; 'SSbD information needs' [80-81,83, 89-91, 102-103, 117-119, 129-135]. The first round of results was screened to identify relevant tools that can be applied for implementing SSbD from a safety and sustainability perspective and from a 'by design' perspective in complex materials such as MCNMs. This resulted in a list of qualitative and quantitative safety and sustainability tools available to address the SSbD profile of chemicals and materials at different stages of the innovation phase (See Supplemental Table 4). A literature search was also performed for SSbD supportive BMs such as 'regenerative business models' and 'circular economy business models.

Thirdly, the ISO 56002:2019 [87] from the literature search was reviewed and used. It provides guidance for the establishment, implementation, maintenance, and continual improvement of an IMS for use in all established organizations and it contains key elements and principles for IM. The ISO Framework was integrated with safety, sustainability, functionality and economic dimensions across the various life stages of a material, chemical, product and process (Supplemental Tables 1-5) to develop the backbone of our conceptual framework. Our methods, analyses and findings were in line with recent systematic reviews focusing on the SSbD construct [137].

Funding Information

This work was performed within the framework of the European Union's Horizon 2020 research and innovation program "SUNSHINE" (Grant Agreement number: 952924) and from the Project Ecosystem for Sustainable Transition in Emilia-Romagna, funded under the National Recovery and Resilience Plan (NRRP), Call for tender No. 3277 of Italian Ministry of University and Research.

Acknowledgment

No

Primary Data

No

Conflict of Interest

The authors declare no conflict of interest.

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A Conceptual Framework for Safe-and-Sustainable-by-Design to Support Sustainable Business Model Innovation and New Product Development

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Supporting Information

Contents

Supplemental Table 1 Overview of regulatory or policy documents relevant for SSbD

Document ID	Description
Chemical Strategy for Sustainability	The EU's chemicals strategy for sustainability towards a toxic-free environment
Zero Pollution Action Plan	Towards zero pollution for air, water and soil
Circular Economy Action Plan	The EU's new circular action plan paves the way for a cleaner and more competitive Europe.
Caldeira et al. 2022a [1]	Safe and Sustainable by Design chemicals and materials Review of safety and sustainability dimensions, aspects, methods, indicators, and tools
Caldeira et al. 2022b [2]	Safe and sustainable by design chemicals and materials - Framework for the definition of criteria and evaluation procedure for chemicals and materials
EC SSbD recommendation	EC Recommendation for safe and sustainable chemicals
Critical raw materials act 2022	The Critical Raw Materials Act should provide a shared understanding of which critical raw materials can be considered as particularly strategic
EcoDesign 2022	Proposal for Ecodesign for Sustainable Products Regulation
Digital product passport	The Ecosystem Digital Product Passport (CIRPASS) prepares the ground for gradual piloting and deployment of the Digital Product Passports (DPPs)
New classification, labelling and packaging (CLP)	Hazardous chemicals – updated rules on classification, labelling and packaging. new hazard classes are: endocrine disruptors (ED) for human health or the environment, persistent, bioaccumulative and toxic (PBT); very persistent and very bioaccumulative (vPvB), persistent, mobile and toxic (PMT); very persistent and very mobile (vPvB).
Product Environmental footprint	Product Environmental Footprint (PEF) is a life cycle assessment based method to quantify the environmental impacts of goods or services
Organisational Environmental Footprint	Organisation Environmental Footprint (OEF) is a multi-criteria measure of the environmental performance of a goods/services-providing Organisation from a life cycle perspective

Supplemental Table 2 Overview of ISO standards supportive of some SSbD aspects

Standard ID	Standard title	STRUCTURE/CONTENT/PROCESS
ISO 62430	Environmentally conscious design (ECD) -Principles, requirements and guidance	PROCESS
ISO GUIDE 64	Guide for addressing environmental issues in product standards	CONTENT
ISO 8887	Technical product documentation - Design for manufacturing, assembling, disassembling and end-of-life processing - Part 1: General concepts and requirements	CONTENT
ISO 17145-1	Ethics assessment for research and innovation - Part 1: Ethics committee	PROCESS
ISO 17145-2	Ethics assessment for research and innovation - Part 2: Ethical impact assessment framework	PROCESS
ISO 17796	Responsibility-by-design - Guidelines to develop long-term strategies (roadmaps) to innovate responsibly	PROCESS
ISO 16649	Managing emerging technology-related risks	PROCESS, STRUCTURE
ISO 12973	Value Management	PROCESS, STRUCTURE
NTA 8287	Safety Cube Method for design, engineering and integration of systems and products	PROCESS, CONTENT
ISO 14020	Environmental labels and declarations - General principles	PROCESS, CONTENT
ISO 14024	Environmental labels and declarations - Type I environmental labelling - Principles and procedures	PROCESS, CONTENT
ISO 14021	Environmental labels and declarations — Self-declared environmental claims (Type II environmental labelling)	PROCESS, CONTENT
ISO 14025	Environmental labels and declarations - Type III environmental declarations - Principles and procedures	PROCESS, CONTENT
ISO 14006	Environmental management systems - Guidelines for incorporating ecodesign	PROCESS, CONTENT
ISO 9001 series	Quality management systems – Requirements	PROCESS, STRUCTURE
ISO 14001	Environmental management systems – Requirements with guidance for use	PROCESS, STRUCTURE
ISO 14032	Environmental management — Examples of environmental performance evaluation	PROCESS, CONTENT

ISO 14033	Environmental management — Quantitative environmental information — Guidelines and examples	PROCESS, CONTENT
IEC 62474	Material declaration for products of and for the electrotechnical industry	PROCESS, CONTENT
IEC 62476	Guidance for evaluation of products with respect to substance-use restrictions in electrical and electronic products	PROCESS, CONTENT
ISO 14063	Environmental management — Environmental communication — Guidelines and examples	PROCESS, STRUCTURE
ISO 26000	Social responsibility	PROCESS, STRUCTURE

Supplemental Table 3 Overview of nano-specific SSbD strategies along all life cycle stages

	Main ambition: *To design nano-specific systems holistically and using life cycle thinking principles to minimise impact on human health and environment*
Dimension	***Life cycle stage (raw materials and resource consumption, production, use, end-of-life)***
Safety dimension (general) [2]:	Minimise or eliminate, where possible, the use of hazardous chemicals/materials in manufacturing processes and Verify possibility of using hazardous chemicals/materials in closed loops when they cannot be reduced or eliminated - Reduce or eliminate exposure to hazardous substances ○ Eliminate or minimise risks through reduction of the use of hazardous substances ○ Analyse and avoid as much as possible the use of substances identified as 'substances of very high concern' (SVHC) ○ Consider value chain-specific regulations ○ Reduction and/or elimination of hazardous substances in manufacturing processes
Safety dimension – nano-specific	Hazard oriented (response): - Resizing: Decrease NMs aspect ratio [3]. - Improve selectivity: NMs designed to be bio-active but not bio-hazardous [4, 5] - Surface modification: · Inorganic to inorganic heterocoagulation / core-shell nucleation [6-12]; · Functional organic coating [13-19] - Doping: Metal substitution of the NMs crystal structure [20, 21] Hazard oriented (dose): - Surface modification: Maximizing functionality/dispersibility, in order to minimizing the required NMs concentration within nano-enabled products [22] Exposure oriented: - NMs immobilization: heterogeneous photocatalysts immobilized [23, 24] - Nano to Micro: granulation /encapsulation techniques [25, 26] - Reduce bio-persistence [27] - Closed system of production (Production phase) - Minimize environmental release during use and disposal of the product - Embedded NM in solid matrix to reduce airborne release
Environmental dimension	- Material efficiency [2]: ○ Maximise yield during reaction to reduce chemical/material consumption ○ Improve recovery of unreacted chemicals/materials ○ Optimise solvent for purpose (amount, typology and recovery rate) ○ Select materials and processes that minimise the generation of waste ○ Minimise the number of chemicals used in the production process

        - Minimize waste generation
        - Identify occurrence of use of Critical Raw Material, towards minimizing or substituting them
- Design for energy efficiency [2]:
    - Select and / or develop (production) processes considering:
        - Alternative and lower energy intensive production/separation techniques
        - Optimize energy efficiency of solvent recovery
        - Maximise energy re-use (e.g. heat networks integration and cogeneration)
        - Fewer production steps (e.g applying lean thinking)
        - Use of catalysts, including enzymes
        - Reduce inefficiencies and exploit available residual energy in the process or select lower temperature reaction pathways
- Use renewable sources [2]:
    - Verify the possibility of selecting feedstocks that:
        - are renewables or secondary materials
        - do not create land competition and / or processes that:
        - use energy resources which are renewable and with low carbon emissions
- Prevent hazardous emissions [2]:
    - Select materials and / or processes that:
        - minimise the generation of hazardous waste and emissions
        - minimise generation of emissions (e.g. Volatile Organic Compounds, acidifying and eutrophying pollutants, heavy metals etc.)
- Design for sustainable packaging and distribution (transport) [28]
    - Minimize distance for distribution (local suppliers)
    - Selecting where possible appropriate or alternative transportation mode (road/rail/water/air)
    - Minimizing product losses and damages by use of appropriate transport packaging
    - Using packaging with maximum efficiency (weight, volume, load/transportation unit, reusability, recoverability)
    - Reusing or recycling packaging material
- Design for end of life [2]:
    - Avoid using chemical/materials that hamper the recycling processes at end-of-life
    - Select processes (and material) that minimise the generation of waste.
    - Employ circularity and circular design indicators [29]
    - Select materials that are (where appropriate):
        - more durable (extended life and less maintenance)
        - easy to separate and sort
        - valuable after their use (commercial after life)
        - truly biodegradable for uses which unavoidably lead to dispersion into the environment or wastewater
- Consider the whole life cycle [2]
    - Consider for example

	▪ Using reusable packaging for the chemical/material under assessment and for chemicals/materials in its supply-chain ▪ Consider the most likely use of chemical/material and if there is the possibility to recycle it ▪ Energy-efficient logistics (i.e. reduction of transported quantities, change in mean of transport) ▪ Reducing transport distances in the supply-chain ▪ Applying responsible sourcing principles - Other strategies [30-34]: o Adopt strategies to maximize the yield of your reaction; promote the re-use of solvents or co-products o Promote the use of certified sustainable raw materials (Critical Materials Act) o Select raw materials and resources that minimize/avoid the production of waste. o Select biobased materials or materials based on secondary feedstock. o Select manufacturing techniques that generate the least emissions, use the least processing aids, use non-hazardous or the least hazardous chemicals or minimized occupational exposure [35]. o Reduction and minimalization of water footprint, ecological footprint, use of critical raw materials**, support downstream resource savings, use of competing renewable raw materials. o Reduction of carbon footprint in all life cycle stages; use of renewable products and greenhouse gas savings downstream; use of renewable energy. o Pollution prevention and control, reduction and minimization of emissions to air, water & soil. o Improved circularity potential (biodegradability of products, waste prevention in the production and use phase, support of recycling opportunities in the value chain, use of recycled materials & feedstock, recyclability, durability, repairability of the material and product). o Take measures to reduce and minimize abiotic depletion, acidification, eutrophication, ozone layer depletion, and photochemical oxidation potential
Social Dimension	Social [30, 31, 33, 34, 36, 37]: - Health and safety: Minimize occupational and consumer health risks: support health & safety of local community's living conditions, safety management a work, management of worker's individual health, product safety, impact on consumer health (see safety – human) - Human rights: Support basic rights & needs including fair wages, appropriate working hours, no forced labor, human trafficking and slavery, no discrimination, social/employer security and benefits, access to basic needs, respect for human rights and dignity. - Social benefit: Contribute to economic and technology development via fostering education, job creation, joint research. - Support skills, knowledge and employability, promotion of skills and knowledge for local community and consumers. - Governance (value chain): promoting value chain with social responsibility [30, 31, 33, 34, 36, 37]. - The SUNSHINE e-infrastructure will adopt to following 19 social sub-categories: child labor, fair salary, working hours, forced labor, equal opportunities/discrimination, workers' health and safety, access to material resources, delocalization and migration, safe and healthy living conditions, respect of indigenous rights, local employment provides important income and training opportunities to community members, supplier chain relations, consumer's health and safety, end-of-life responsibility, contribution to economic development, prevention and mitigation of armed conflicts, technology development, corruption and ethical treatment of animals [37].

Economical Dimension	Economical [30, 31, 33, 34, 37] - Life cycle costing (LCC): total cost over the life cycles the product. It can include Externality cost (e.g. the costs associated with environmental emissions, worker safety, and health protection, and land eco-remediation - Functionality (optimize product performance) - Optimize product cost (purchase and production cost) Optimize profitability (added value, net present value, financial profit and payback period) [30, 31, 33, 34, 37]

*particularly CMR, Carcinogenic, mutagenic and reprotoxic; ED, endocrine disruption; PBT, persistent, bioaccumulative and toxic; vPvB, very persistent and very bioaccumulative; and SVHC, substance of very high concern.

**Critical raw materials (europa.eu)

**Responsibly sourced materials (JRC Publications Repository - Responsible and sustainable sourcing of battery raw materials (europa.eu)

Supplemental Table 4. Information needs to assess safety, sustainability, functionality and economic dimensions across the various life stages of a material, chemical, product and process as Guidance to integrate SSbD in IM principles; many adapted from the Early4AdMa brochure [38].

Integration of IM with SSbD following LCT principles **IM element: PLANNING** **Embed safety and sustainability criteria within the IM system.** **IM element: OPERATIONS** **Implement safety and sustainability concepts during the innovation process.**			
Safety impact assessment aiming at minimizing human health and environmental impacts [2, 39, 40].	Environment impact assessment aiming to minimizing the environmental footprint [2, 30, 31, 33, 34, 38].	Social impact assessment aiming to improve the social aspects (worker, local communities, consumers and society as a whole) [30-34].	Functionality + Economic impact assessment aiming at optimizing economic feasibility and societal value [30, 31, 33, 34, 40].
Hazard characterization/assessment - Human toxicity: are there any legislative restrictions? Are there any hazardous properties identified in REACH, CLP? Is there any ecotoxicological (potential accumulation/persistency) information (e.g. basic information on potential ecotoxicity, read across data) in scientific literature? - How are the chemical components or the (pristine) nanomaterial labelled? Are there any CMRs, ED or SVHC**? Are there any restrictions? - Physicochemical characterization: primary/constituent particle size (within the nanoscale range and aspect ratio). - Does it look like asbestos fibres (HARN)? Shape (sphere, rod, fibre, etc.). - Is the chemical or nanomaterial bio-persistent? Solubility (highly soluble: e.g. sea salt, soluble: e.g. Ag NPs, insoluble: TiO2 NPs, or highly insoluble: e.g. CNTs).	Raw Materials and resources - Are critical raw materials^ used? - Are the raw materials used classified as hazardous or persistent (CLP)?^^ (Avoid the use of hazardous or persistent substances, as they may circulate or hamper the re-use potential of materials or products). - Does the process of extracting the raw materials require high energy, water, or land consumption and/or have an impact on global warming potential (emission of greenhouse gases)? Manufacturing production, transport and use	- Is customer protection (health & safety of local community's living conditions, product safety, impact on consumer health) considered? - Is Occupational health & safety Health & Safety (occupational health risks, safety management a work, management of worker's individual health, (see safety – human) considered? - Human and labor rights/basic rights & needs (fair wages, appropriate working hours, no forced labor,	- Is required functionality & selected extraction methodology linked with the lowest possible toxicity, environmental & sustainability impacts? - Is the product Profitability (social and economic value, net present value, financial profit, payback period) adequately met? - Have life cycle cost & externalities (a cost or benefit caused by a producer that is not financially incurred or received by that producer) of the product been taken into account? - Are the market-related criteria (stakeholder expectations and product performance) adequately met?

- What is the toxicity of the chemical or (pristine) nanomaterial?* (in vitro and in vivo toxicity test are performed) - What is the reactivity, accumulation, immunotoxicity, and/or genotoxicity of the pristine or similar (N)Ms or other relevant NMs* - What is the toxicity of the aged / transformed material? - Which transformations of the NM can be expected throughout the life cycle (focus on dissolution, aggregation, agglomeration)?*** - How are chemical components of the doping, coating, surface treatment or other functionalization labelled? What is the CLP of the different crystalline forms? Chemical composition of the doping, coating, surface treatment or other functionalization. - Toxicity, C&L of these chemical components. - Is it possible to use read across or grouping of relevant forms to fill remaining data gaps for risk assessment?[###] Exposure characterization / assessment - What is the intended formulation and the potential exposure route and population? - Which transformations of the NM can be expected throughout the life cycle (focus on dissolution, aggregation, agglomeration)?*** - Which types of exposure and release scenarios can be expected? Qualitative description of intended material production process, product production and after use. - Occupational exposure measurement (measures workers exposure concentrations. - What are relevant exposure reduction measures? Assessment of relevant exposure reduction measures and their efficiency. - What is the outcome of the risk assessment of the relevant nanoforms for the relevant exposed populations throughout the life cycle of the product? What are the uncertainties in this assessment? Are there still important data gaps (e.g. advice for further testing)?[####]	- Does the process of manufacturing, production, transport, use and/or consumption require high energy or land consumption and/or have an impact on global warming potential (emission of greenhouse gases)? - Can the production process be energy and water efficient? - Is there a high amount of waste in the process of manufacturing and production? - Is the waste generated during manufacturing, production, transport and use recyclable or reusable? - Does the emission and waste generated during manufacturing, production, transport and use, contain persistent or hazardous substances? - Do the manufacturing processes use a high volume of solvents? - Do the manufacturing processes of manufacturing and production use a high volume of water? - End-of life (Recyclability and re-usability) - Can the raw material in the application context be	human trafficking and slavery, no discrimination, harassment prevention, social/employer security and benefits, access to basic needs, respect for human rights and dignity). - Supply chain responsibility, (community engagement, local employment, safe and healthy living conditions, transparency and responsible communication, consumer product experience, end-of-life responsibility) - Contribution to economic and technology development (education, job creation, joint research) - Skills & knowledge (skills, knowledge and employability, promotion of skills and knowledge for local community and consumers)	- Is there transparency and availability of information on the product? - Is there value chain collaboration for Life Cycle Thinking to be implemented effectively? - Is the business model circular? - Are any Substances of Concern justified from an Essentiality perspective? - Is the quality of the production process sufficient? Are the physicochemical properties reproducible and low batch to batch variability?

- Does occupational exposure increase due to the upscaled process? Update of relevant exposure reduction measures in occupational setting in response to up scaling.
- Is there a Mobility/Public health exposure concern?
Safety (environment) aiming at minimizing environmental impact
- Ecotoxicity: NM legislative restrictions REACH, CLP.
- Ecotoxicological (potential accumulation/persistency) information (e.g. basic information on potential ecotoxicity, read across data) in scientific literature.
  - Ecotoxicological information (specific information on potential acute & chronic ecotoxicity, potential bioaccumulation.
  - In vivo acute & chronic ecotoxicty test on algae, crustacean and fish Ecotoxicological information: Growth inhibition in aquatic plants, In vitro tests using relevant cell lines: cytotoxicity assays for metabolic activity, membrane integrity, lysosomal function. Biopersistency and biodurability.
	recycled, re-used or recovered?
	- Is the recycling process efficient? (i.e. is volume and quality of recycling product sufficient for a circular economy?)
	- Is there an efficient system in place to recycle the products? Or is there a concept or plan to recycle the material/recover the individual materials?
	- Does the process of recycling require high amounts of energy, water, or land consumption and/or have an impact on global warming potential (emission of greenhouse gases)?
	- Is it possible to re-use (most of) the materials in the same or another function?
	- Are different components used that are integrated, which might make recycling technically difficult?
	- Is the application of the material or product durable e.g. long-term functionality, or reparable? (Durable indicates that there is long-term functionality)
	- Does the application of the material or product protect & restore biodiversity and ecosystems services?		

C&L, Classification and labelling; [C&L Inventory - ECHA (europa.eu);](C&L Inventory - ECHA (europa.eu))
NM: nanomaterial

* Physicochemical properties of NM (e.g. as obtained from manufacturing): primary particle size, shape, dissolution rate (water) and surface chemistry. Toxicity, C&L of the NM or similar (N)Ms.
**CMR, Carcinogenic, mutagenic and reprotoxic; ED, endocrine disruption; SVHC, Substance of very high concern
*** Physicochemical properties of the NM throughout the life cycle of the product: primary, aggregated and agglomerated particle size, surface chemistry and dissolution rate (relevant media) (experimental or else theoretical information).
**** Please, select the most important endpoints based on the type of NM and expected exposure. Hazard information on the reactivity, absorption (e.g. in vitro cellular uptake or barrier crossing), immunotoxicity and/or genotoxicity of the pristine or similar NMs (experimental or else theoretical information).
# Exposure scenarios of hotspots and associated forms of NM throughout the production process and downstream use of the products, including waste disposal (theoretical information).
Please, select the most important endpoints based on the type of NM and expected exposure. Hazard information on the reactivity, absorption, immunotoxicity and/or genotoxicity of the exposure relevant nanoforms or similar NMs for the exposed populations (experimental or else theoretical information).
Earlier obtained information for read across or grouping as described in the ECHA guidance (i.e. phys-chem and in vitro data of relevant nanoforms and phys-chem and hazard information of similar nanoforms).
Earlier obtained information for the risk assessment of all relevant nanoforms for all relevant exposure scenarios (e.g. exposure quantities of relevant exposure scenarios and hazard information on relevant or similar nanoforms)
^Critical raw materials (europa.eu)
^^CLP Legislation - ECHA (europa.eu)

Supplemental Information and Table 5: Multicomponent nanomaterials as a case study to gather lessons learned for theoretical framework on how to integrate SSbD to IM following LCT principles

Currently, one of the greatest challenges of NM safety assessment is the rapid and diverse development, and wide-ranging complexity of emerging manufactured NMs, which consist of multiple conjugated components, such as in the case of MCNMs [41-44]. As these materials consist of several components (e.g. linkage of several nanomaterial types and forms, and/or nanomaterial-chemical combinations) an improved understanding is needed of how these components interact with each other, with other NMs and/or chemicals leading to mixture toxicity, since unknown interactions may result in synergism, potentiation or antagonism of hazards. Additionally, there is a need to establish potential release of components from the MCNMs in the form of fragments and/or dissolution and transformation of the materials in physiological media and biological compartments. This combined information is necessary to identify which of the MCNMs components and physicochemical attributes are responsible for any observed hazard responses. Consideration should also be given to establishing how the identities of the MCNMs and the products incorporating them change throughout their full lifecycle, spanning release, weathering and aging at different stages from manufacturing, to use and end of life. This will vary according to the MCNM use scenario (e.g. consumer product, *versus* medical use; indoor *versus* outdoor use), which will have a substantial impact on potential transformations of the MCNMs physicochemical characteristics throughout different stages of the lifecycle. Filling the gaps in our knowledge will be central to facilitating the implementation of improved LCT SSbD approaches. Similar considerations apply to the assessment of the environmental safety of MCNMs. Environmental safety assessment often requires assessment of the impacts of MCNMs on real-world ecosystems derived from the toxicity testing of a limited set of test species of different trophic levels (often three levels are considered: primary producers like plants and algae, primary consumers like daphnids, and predators like fish). When the availability of toxicity data is limited to apical endpoints like growth inhibition, reproduction, and mortality, so-called extrapolation factors are applied to account for uncertainties related to the extrapolation of this data to impacts on ecosystems. The preferred way of performing environmental safety assessment is on the basis of toxicity data for a somewhat bigger number of organisms/plants. In this case the so-called Species-Sensitivity Distribution for a specific MCNMs can be generated, taking account of interspecies variability in sensitivity [45]. The Species-Sensitivity Distribution approach is a statistical approach which requires a minimum of roughly 8-10 toxicity data for different organisms. The data are used to generate a cumulative distribution of the sensitivity of organisms to a contaminant. This distribution is subsequently used to derive the concentration of a contaminant that is predicted to be protective of 95 % of the species in an ecosystem [45].

The safety of MCNMs can be addressed by the following aspects:

1) "*What they are: Physicochemical identity*", specifically characterizing the properties of pristine (as originally manufactured) materials and extrinsic physicochemical material properties in relevant environmental and biological media (e.g., particle size distribution, sedimentation rate, surface composition, dissolution rate, reactive species and pro-oxidative potential);

2)"*Where they go: Environmental fate, human biodistribution and exposure*", including effective exposure and uptake dynamics;

3) "*What they do: Human and environmental toxicity*" [46].

The information required to outline the safety profile of MCNMs and materials throughout all life cycle stages [39, 40] is summarized in Supplemental Table 3. Addressing safety at the different stages of the innovation process in the context of SSbD for NMs can be performed by using both qualitative and quantitative tools [40, 47]. The list of tools that can be used to address NM safety is provided in *Table* . The tools have different domains of application (i.e. medical devices, chemical substances, cosmetic product, drugs, food labelling) mostly addressing dermal, oral and inhalation as main routes of exposure, and worker, consumer and environment as target population. A detailed description of the above listed tools is out of scope of this article, yet further information can be found on the RIVM web page : https://www.siatoolbox.com/tool and in Soeteman-Hernández et al. [47]

In the context of chemicals, sustainability can be seen as the "*ability of a chemical, material, product or service to deliver its function without exceeding environmental and ecological boundaries along its entire life cycle, while providing welfare and socio-economic benefits"* [2]. SSbD following LCT principles aims to address three pillars of sustainability (environmental, social and economic):

1. Minimizing raw materials and resources (water, solvent, land consumption), minimizing waste, and minimizing the environmental footprint during design, manufacturing, production, transport, use and end-of-life [38]
2. Improving social benefits, and
3. Optimizing economic feasibility, viability and value [2]

Table illustrates an overview of tools that can be used to assess sustainability for MCNMs. Additional tools can be found in: RIVM Sustainability method selection tool

A challenging aspect for applying SSbD across the innovation chain is the consistency of the results. Results from evaluation at lower Technology Readiness Levels should not be considered as conclusive due to several assumptions and high uncertainty in these models. Rather, incorporating SSbD within the design process should be viewed as an evaluation of a scenario based on best available knowledge in the innovation process.

Table 5. Qualitative and quantitative safety and sustainability tools available to address the SSbD profile of nanomaterials (and possibly MCNMs) at different stages of the innovation phase. Most tools and methods need to be adapted for MCNM.

Safety		Sustainability			
Qualitative Tool/ Innovation Stage	**Quantitative Tool/ Innovation Stage**	**Method**	**Description**	**Innovation stage**	**Impact categories**
CENARIOS Risk management and monitoring system *Early phase*	SimpleBox4Nano: screening fate assessment model (semi-quantitative) *Midterm and late phase*	Environmental Life Cycle Assessment (E-LCA) [48, 49]	A systematic approach for the assessment of the environmental impacts of products along their entire life cycle, from design to end of life. In the context of SSbD	Early Tool: LICARA nano-SCAN [50] Type of data required: qualitative or semi-quantitative Limitations: limited economic and social criteria and aspects such as criticality and circularity are not accounted for.	Climate change, human toxicity (cancer), human toxicity (non-cancer), eco-toxicity, particulate matter, ionizing radiation, ozone depletion, eutrophication (terrestrial, fresh water, and marine), ozone formation, acidification, fossil resources and mineral and metal resources
Consexpo Nano Tool *Early, midterm and late phase*	NanoRisksCat *Early and midterm phase*	Socio-Economic Analysis (SEA) [37, 40, 51, 52] Social-LCA [32, 53, 54].	S-LCA provides information on social and socio-economic issues for decision making, promoting reflection, dialogues on the social and socio-economic aspects of productions and consumption of the performance of an organization [32, 37, 50, 52-54]. General impact categories: Consumer protection Occupation health and safety Human and labor right Supply chain responsibility	Early and throughout the entire lifecycle Tool: semi-quantitative tool for initial screening and socio-economic assessment of (advanced) engineered NMs and nano-enabled products [37, 50, 52].	Tool contains nineteen impact subcategories pertaining to various stakeholder groups (workers, local community, value chain actors, consumers and society as a whole) including child labor, fair salary, working hours, forced labor, equal opportunities/discrimination, workers' health and safety, access to material resources, delocalization and migration, safe and healthy living conditions, respect of indigenous rights, local employment provides important income and training opportunities to community members, supplier chain relations, consumer's health and safety, end-of-life responsibility, contribution to economic development, prevention and mitigation of armed conflicts, technology development,

Safety		Sustainability			
Qualitative Tool/ Innovation Stage	**Quantitative Tool/ Innovation Stage**	**Method**	**Description**	**Innovation stage**	**Impact categories**
					corruption and ethical treatment of animals [37, 50, 52].
Stoffenmanager *Early phase*	Stoffenmanager Nano (semi-quantitative) *Early and midterm phase*	Life cycle costing (LCC) [37, 50, 55, 56] LICARA NanoScan	LCC considers all the costs that will be incurred during the lifecycle of the product or service	Early and throughout the entire lifecycle Tool: semi-quantitative tool for initial screening and socio-economic assessment of (advanced) engineered NMs and nano-enabled products [37, 57].	Profitability, market-entry criteria; Acquisition costs, Installation costs, Operation and Maintenance costs, End of Life costs, Residual value
GUIDEnano *Early, midterm and late phase*	Swiss precautionary matrix *Early and midterm phase*				
LICARA NanoScan *Early and midterm*	Nanosafer CB tool *Midterm and late phase*				
ANSES: Control banding tools for NMs	Health Impact Assessment (HIA) under REACH *Midterm and late phase*				
MARINA Risks assessment strategy *Early and midterm phase*	RISKOFDERM *Early and midterm phase*				
ECETOC's NanoApp *Early and midterm phase*					

Obtaining relevant and reliable safety and sustainability data for MCNMs is not easy and more research is needed.

From a *MCNMs safety perspective*, most hazard characterization and risk assessment approaches have been developed and tailored for first-generation, pristine and/or simple NMs, with significant knowledge generated through the NanoSafety Cluster projects on characterization and hazard testing. However, their performance has not been evaluated for reliable reporting on more complex, industrially relevant NMs that consist of multiple components. Thus, it is necessary to appraise the current nano-specific safety testing methods to determine if they are also applicable to more complex MCNMs, or if they need to be adapted. Thus, experimental approaches will need to be tailored towards assessing the potential for mixture effects. This will provide appropriate data sets that will underpin the development of SSbD strategies for MCNMs and mixtures of MCNMs and chemicals, but requires time and effort. In addition, the use and application of more optimal testing strategies will contribute to improved ethical consideration of animal use through promoting the application of *in silico*, *in vitro* and improved *in vivo* studies (e.g., use of *in vitro-in vivo* extrapolation to remove need for *in vivo* dose range finding), ultimately leading to the Reduction, Refinement and/or Replacement of animal testing (3Rs). A list of information requirements to address the safety of MCNMs is reported in Table 2. However, for MCNMs additional safety issues due to their multicomponent nature may trigger further specific information needs. Identifying and acquiring all this information is a complex and time- and cost consuming process. Despite the efforts taken in past decades to address the toxicity and exposure of manufactured NMs, gaps in knowledge and tools still exist and are seen as a bottleneck to address the human and environmental risks of NMs [58].

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