



Safety and sustainability by design: An explorative survey on concepts' knowledge and application

Veruscka Leso^{a,1}, Tomas Rydberg^{b,1}, Maja Halling^b, Spyros Karakitsios^{c,d}, Fotini Nikiforou^{c,d}, Achilleas Karakoltzidis^{c,d}, Denis A. Sarigiannis^{c,d,e,f}, Ivo Iavicoli^{a,*}

^a Department of Public Health, Section of Occupational Medicine, University of Naples Federico II, Via S. Pansini 5, Naples 80131, Italy

^b IVL Swedish Environmental Research Institute, Sweden

^c HERACLES Research Center on the Exposome and Health, Center for Interdisciplinary Research and Innovation, Aristotle University of Thessaloniki, Thessaloniki, Greece

^d Environmental Engineering Laboratory, Department of Chemical Engineering, Aristotle University of Thessaloniki, Thessaloniki, Greece

^e National Hellenic Research Foundation, Athens, Greece

^f University School of Advanced Study IUSS, Pavia, Italy

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ABSTRACT

The Safe and Sustainable by Design (SSbD) concept integrates safety and sustainability of chemicals and materials, throughout their entire life cycle and minimizes their environmental footprint. The European Commission (EC) in 2022 developed a framework to practically apply SSbD. This study investigated the knowledge on SSbD and the operationalization of such framework among the partners of the Partnership for the Assessment of Risks from Chemicals (PARC) program. Forty-one responses from 32 PARC Institutions were collected through a 21 item-online survey. Seventy-three % of the respondents had knowledge of SSbD, although only 49 % reported to have been directly engaged into SSbD projects. The EC-SSbD framework was applied by the 26 % of participants and in 47 % of cases it included a (re)design phase. With respect to the safety and sustainability, the assessment of the hazard, the human health and safety aspects in the production and processing, and the human health and environmental aspects in the final application of the chemical/material was addressed by the 74 %, 52 % and 65 % of the respondents. Lower percentages of positive responses regarded the environmental, social and economic sustainability assessment: 35 %, 20 % and 13 %, respectively. Overall, while the framework provided the necessary building blocks and opportunities for SSbD, concerted and iterative Research, Industry, and Academia efforts are necessary to develop/improve assessment methods, models and tools to make SSbD as an approach to chemical risk assessment and management to protect human health and the environment, and ensure to operate within the planetary boundaries.

1. Introduction

With the European Green Deal, the European Commission (EC) aims to transform the EU's economy for a more sustainable future (EC, 2019), focusing on climate, biodiversity, circularity as well as improving measures for protecting human health and the environment. This is part of an ambitious approach to tackle pollution from all sources and move towards a zero-pollution economy for a toxic-free environment. The above, are fully in line with the EC Chemicals Strategy for Sustainability (CSS), published in 2020, aiming at human health and environment protection, while Safe and Sustainable by Design (SSbD) is a key pillar

towards this direction (EC, 2020a). According to the CSS: "SSbD can be defined as a pre-market approach to chemicals that focuses on providing a function (or service), while avoiding volumes and chemical properties that may be harmful to human health or the environment, in particular groups of chemicals likely to be (eco) toxic, persistent, bio-accumulative or mobile. Overall sustainability should be ensured by minimizing the environmental footprint of chemicals in particular on climate change, resource use, ecosystems and biodiversity from a life cycle perspective" (EC, 2020b). The concept promotes such a holistic approach that integrates safety and sustainability of chemicals and materials, throughout their entire life cycle and minimizes their environmental footprint

* Corresponding author.

E-mail address: ivo.iavicoli@unina.it (I. Iavicoli).

¹ Equal contribution

(Caldeira, 2022a).

Finding strategies to practically apply SSbD is an issue currently addressed by policy, academic, and industrial players around the EU (Sudheshwar et al., 2024). SSbD is proposed to develop into a voluntary action that supports current regulations such as the Registration, Evaluation, Authorization, and Restriction of Chemicals (ECHA, 2024), the Corporate Sustainability Reporting Directive (EC, 2023), the EU taxonomy (European Commission, 2020b), and the Sustainable Product Initiative (EC, 2020c). To fulfill these ambitions, the EC developed a framework for the definition of criteria for SSbD chemicals and materials that was announced in a Commission Recommendation of the 8th of December 2022 (EC, 2022).

The framework encompasses both safety and sustainability assessment, and aims to steer the innovation process towards the green and sustainable industrial transition; substitute or minimize the production and use of substances of concern, in line with, and beyond existing and upcoming regulatory obligations; minimize the impact on health, climate and the environment during sourcing, production, use and end-of-life of chemicals, materials and products (EC, 2022b; OECD, 2020).

The framework is composed of two components: a (re)design phase in which design guiding principles and indicators are proposed to support the design of chemicals and materials, and a safety and sustainability assessment phase in which the safety, environmental and socio-economic sustainability of the chemical/ material are assessed. The stepwise approach for the safety and sustainability assessment, is composed of different steps:

- Step 1: Hazard assessment of the chemical/material, that looks at the intrinsic properties of the chemical or material in order to understand its hazardous profile;
- Step 2: Human health and safety aspects in the chemical/material production and processing phase, referring to occupational health and safety aspects from raw material extraction to production of the chemical or material including recycling or waste management;
- Step 3: Human health and environmental aspects in the final application phase, that relies on evaluating whether the final use of a chemical or material poses any risk to human health or the environment;
- Step 4: Environmental sustainability assessment, assessing the impacts along the entire chemical/ material life cycle (e.g., on climate change and resource use).

A fifth step addressing the social and economic sustainability assessment along the chemical life cycle has been proposed although it is in a still under exploration. This step may include the evaluation of a variety of aspects, such as equity/equality, human wellbeing, human rights, livelihood, the attention to the local context and governance and the integration of different stakeholders and community perspectives, together with the assessment of the possibility to achieve an economic growth considering the resource-constrained world's environmental and social implications (e.g. product cost, profitability, life cycle cost, and market-related criteria) (Caldeira et al., 2022b)

Case studies have been already conducted by the EC's Joint Research Centre (JRC) (Caldeira et al., 2023) to test the applicability of the SSbD framework. Some practical challenges emerged from this first exercise. However, the SSbD framework provides a first attempt to combine assessment building blocks from the perspective of safety, sustainability and socio-economic assessment. Moreover, the comprehensive nature of the framework, although promising in the future is time-consuming and expensive in the short term and demands a high level of expertise for the SSbD assessment (Sudheshwar et al., 2024). In this view, although the need for an SSbD approach for chemicals, materials and products has been extensively discussed in the scientific community, no literature data are currently available on awareness and practical applicability of the more recent framework promoted by the EC in the framework of an international setting of researchers involved in chemical risk assessment

and management.

Therefore, our study aimed at mapping and analyzing the current knowledge on the SSbD concepts and the operationalization of the EC framework in case studies among the scientific community engaged in the Partnership for the Assessment of Risks from Chemicals (PARC). PARC is an EU-wide research and innovation partnership program, aimed at supporting EU and national chemical risk assessment and risk management bodies with new data, knowledge, methods, networks and skills to address current, emerging and novel chemical safety challenges (Marx-Stoelting et al., 2023).

2. Methods

2.1. The investigated population and data collection

A "PARC internal survey on Safe and Sustainable by Design case studies" was conducted between the 20th of April and the 30th of June 2023. It has been performed among the activities of the Work Package 8 - Concepts and toolboxes; Task 8.1, SSbD; Activity 8.1.3 SSbD toolbox operationalization: Use cases & indicators. Specific aims of the activity included the identification of the most relevant use cases to explore different types of applications of the SSbD, to test the methodology developed by the EC and to supplement the use cases developed by the EC. In this scenario, the survey was developed with the aim to achieve valuable inputs from PARC participants for the SSbD use cases inventory, with the additional purpose to identify criteria for setting suitable PARC case studies to test the operationalization of the toolbox developed under the 8.1.2 Activity.

All the partners engaged in the PARC Consortium were asked to participate in the survey completing a specifically targeted questionnaire via Google form. The survey was accompanied by a letter explaining the aims of the research and how the information collected could be useful for the scopes of the PARC project. In any case, voluntary participation was assured by all the co-leads of the 8.1.3 promoting task. No exclusion criteria were applied to the participation. The collected information has been treated confidentially according to the requirements of the General Data Protection Regulation (GDPR). Data obtained from this survey have been saved, stored, and processed by the 8.1.3 activity co-leads.

2.2. The "PARC internal survey on safe and sustainable by design case studies"

The survey was developed by the PARC task 8.1.3 co-leads to collect information concerning knowledge regarding the SSbD concepts and possible application into projects or specific case studies, together with data on the operationalization of the EC framework. It consisted of 21 items divided into multiple choices and open questions and required, in total, about 15–30 minutes to be completed. The survey included a first section focused on the respondent information, including affiliation category (Private companies, Research Institutions, Universities) and the geographical origin of the participants. The knowledge on the SSbD concept was explored through a yes/no question. The direct involvement of the respondent into any project applying safety and sustainability aspects into the development of materials, products or processes was also investigated through a yes/no item. The priority sectors addressed by the above-mentioned project were also asked. The categories proposed in the survey were extrapolated from the priority sectors listed in the EC recommendation and in the JRC reports: textiles, food contact materials, information and communication technologies, construction materials, low-carbon mobility, batteries or renewable energy sources; cosmetics, and others. The survey also explored whether the participants applied the SSbD framework proposed by the EC or any other SSbD framework, as well as in which use cases/case studies these were applied and which were the chemicals/materials investigated. As regards the framework components, specific items explored whether the

case/study included a (re)design stage for chemical or materials and which principles have been followed in such phase. Specifically focusing on the safety and sustainability assessment, yes/no questions were included to understand whether the case study included a hazard assessment for chemicals and materials; human health and safety aspects of production and processing; human health and environmental aspects in the final application phase of the chemical/material in question; an environmental, social and economic sustainability assessment.

3. Results

Forty-one responses were received for the survey. Twenty-nine (70 %) from representatives of Research Institutions and 12 (30 %) from University researchers. Overall, these responses come from 32 out of the 201 Institutions participating in PARC (16 %). The geographical spread of the respondents was wide, with 1 or 2 respondents per country

(Fig. 1).

At the general question “Do you have knowledge about the safe and sustainable by design concept?”, in 30 responses (73 %), the participants reported a positive response meaning that awareness on the SSbD concept was quite widespread among the investigated sample (Table 1).

However, only 20 respondents (49 %) reported any knowledge of or direct engagement into projects applying safety and sustainability aspects into the development of materials, products or processes.

In terms of projects' priority sectors, 27 responses were collected. Among those, the most frequently reported sector of application was the food contact materials (8 responses; 30 %). In only two cases, respectively, batteries or renewable energy sources (7 %), and cosmetics (7 %) were mentioned as fields of SSbD interest. A miscellaneous of other fields have been reported in 15 additional responses (56 %), including recycling of plastics, chemicals in utensils, pharmaceuticals, drinking water production, epoxy resins, sprays/paints, and nano-medicine (Fig. 2).



Fig. 1. Number of responses retrieved for country.

Table 1
Number of responses retrieved for item.

Survey item	Number of retrieved responses for item	Yes n. (%)	No n. (%)
Do you have knowledge about the “safe and sustainable by design” concept	41	30 (73 %)	11 (27 %)
Do you know or are you directly involved in any project applying safety and sustainability aspects in the development of materials, products or processes?	41	20 (49 %)	21 (51 %)
Have you applied the SSbD framework proposed by the European Commission in your work?	35	9 (26 %)	26 (74 %)
Have you applied any other SSbD tools in your work?	34	10 (29 %)	24 (71 %)
Does your use case/case study include a (re)design stage for chemicals or materials?	30	14 (47 %)	16 (53 %)
Does your use case/case study include a hazard assessment for chemicals and materials?	31	23 (74 %)	8 (26 %)
Does your use case/case study include human health and safety aspects of production and processing?	31	16 (52 %)	15 (48 %)
Does your use case/case study include human health and environmental aspects in the final application phase of the chemical/material in question?	31	20 (65 %)	11 (35 %)
Does your use case/case study include an environmental sustainability assessment?	31	11 (35 %)	20 (65 %)
Does your use case/case study include a social sustainability assessment?	30	6 (20 %)	24 (80 %)
Does your use case/case study include an economic sustainability assessment?	31	4 (13 %)	27 (87 %)

Priority sectors of SSbD projects

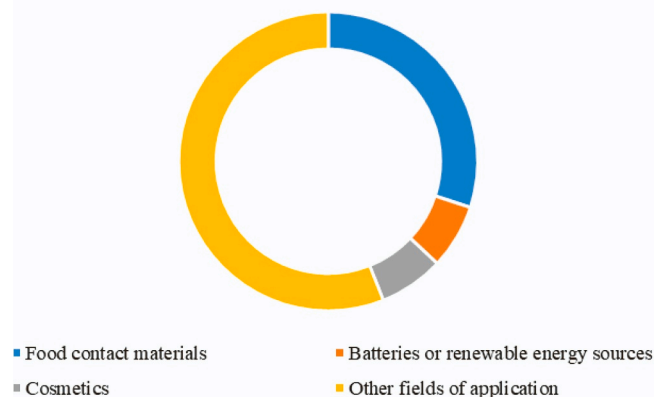


Fig. 2. Priority sectors of SSbD projects.

In only 9 responses (26 %), participants declared to have applied the EC SSbD framework in their projects, and a comparable percentage of responses (10 %) reported the employment of other SSbD tools. Seventeen responses were provided on specific use case/case studies on SSbD in the above-mentioned projects. These use cases specifically regarded plasticizers in flooring materials, plastic additives, recycling plastics, PFOS, cosmetics and food contact materials, high-performance large area organic perovskite devices for lighting, energy and pervasive

communication; energy storage systems in green and circular economy, materials for solar desalination devices, nanomaterials and nanocellulose. Concerning the chemicals/materials addressed in the use case/case studies: bisphenol A alternatives, different plasticizers, graphene, metal oxides, carbon nanofibers, titanium dioxide, silica dioxide, zinc oxide, lipid based nanoparticles, silica nanobeads; advanced materials, including biocides, paint formulations, papermaking, catalysts and facade insulation, and perovskites have been reported.

Forty-seven% of the responses indicated that the use case/case study included a (re)design phase (Table 1). Principles addressed in the case study were primarily (21 responses retrieved): to minimize the use of hazardous chemicals or materials (43 %) followed by considering the whole life cycle of chemicals, materials and products (14 %); preventing and avoiding hazardous emissions (9 %) and considering the material efficiency (4 %). In some cases, respondents indicated that a series of principles have been considered without a suitable detail (30 %).

With respect to the safety and sustainability assessment (Table 1; Fig. 3), 74 % of the retrieved responses reported that the use case/case study under investigation included a hazard assessment step. Human health and safety aspects of production and processing were reported to have been included in 52 % of the responses; 65 % reported the inclusion in case studies of a specific focus on human health and environmental aspects in the final application phase of the chemical/material in question. More limited percentages of responses, 35 %, 20 % and 13 % resulted positive with respect to the inclusion of an environmental, social and economic sustainability assessment, respectively.

4. Discussion

This pilot study represents the first attempt to address the knowledge on SSbD concepts among partners of the European PARC project and the application of the EC SSbD framework in case studies outside PARC.

Concerning the collected response rate, only 32 out of 201 institutions engaged in PARC participated into the survey (16 %). This low rate of response may be related to the unfamiliarity of the overall PARC partners with respect to the SSbD concept. In fact, multiple aspects of the chemical risk assessment, also different from the SSbD approach, are addressed in the various PARC work packages, thus limiting the number of those partners dedicated to the SSbD operationalization. This may have prevented a greater participation of partners due to the diverse priority areas of research.

Interestingly, most of the respondents (73 %) reported to have knowledge on the SSbD concept, although less than a half of them (49 %) declared to have been involved into the practical application of such concepts in the development of materials, products, or processes. Additionally, although there was a general awareness concerning the SSbD, a limited rate of participants (26 %) reported applying the EC framework in their projects. This may be explained by the fact that the SSbD framework was announced by the EC in the Recommendation of the 8th of December 2022, and our survey started only 4 months afterwards. This timeframe may be considered too short to allow Research Institutions and Universities a formal operationalization of the framework. Longitudinal studies on all these aspects could be helpful in understanding how the wide spreading of the SSbD concepts and the increasing awareness of the scientific community on such approach and its application into the chemical risk assessment and management processes may change the obtained results.

Additionally, although the framework may be beneficial for long-term societal and environmental wellbeing, its comprehensive nature demands a high level of expertise combined with multiple scientific domains as well as elevated costs for its application that could have functioned as obstacles to its prompt application (Sudheshwar et al., 2024). This may be the case of both small medium enterprises, that often face resource, personnel and time restrictions, but also of large companies that may suffer from the SSbD hazard-based restrictions in the use of most dangerous chemicals that are used otherwise precisely for their

Safety and sustainability assessment

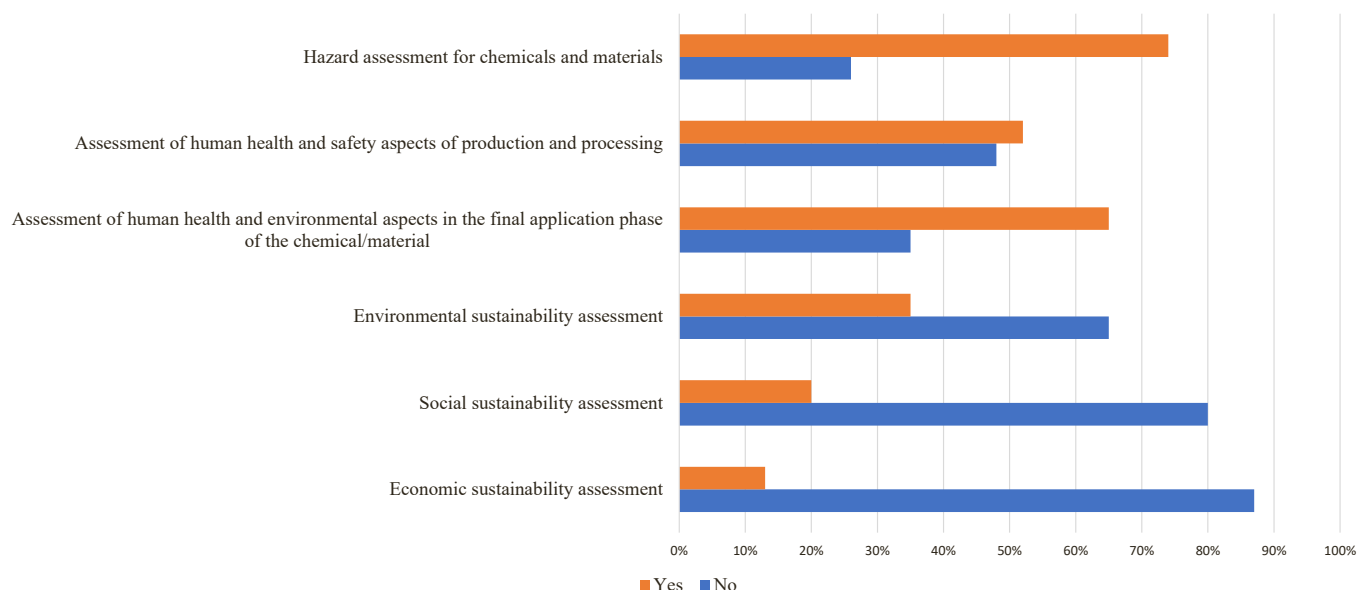


Fig. 3. Safety and sustainability assessment.

inherent toxic functionality. In this view, future investigation should be focused at defining strategies and tools that promote the use of New Approach Methodologies (NAMs) and artificial intelligence for the EC framework application that need to be rapid, cost-effective, and accepted by regulatory and industry communities, nongovernmental organizations, and the public.

Interestingly, although a limited number of positive responses were retrieved concerning the application of the EC framework, a greater number of respondents declared to have been engaged into the hazardous assessment steps of the same framework. This suggests that some kinds of assessment, particularly those related to the safety evaluation of chemicals, products and processes have been done in several projects, apart from the pathway proposed by the EC. Regarding the percentages of responses relative to the application of the different safety and sustainability framework's steps into case studies, some interesting results emerged. In fact, while more than a half of the respondents reported that the use case/case study under investigation included an hazard assessment step, an evaluation of human health and safety aspects of production and processing and an evaluation of human health and environmental aspects in the final application phase of the chemical/material in question; more limited percentages of responses, one third or less, resulted positive with respect to the inclusion of an environmental, social and economic sustainability assessment.

Overall, this may suggest that efforts made on health and safety are different to those devoted to sustainability. Safety by Design aims at addressing safety issues already during the research and development and design phases of new technologies. The Safety by Design has increasingly become popular in the last few years for addressing the risks of emerging technologies like nanotechnology and synthetic biology (van de Poel and Robaey, 2017). Additionally, the common idea that safety can also harm the environmental, economic, and social pillars of sustainability, may be at the basis of the retrieved discrepancies. Linking safety and sustainability is not a novel idea. Scientific evidence, in fact, suggests the importance of safety in supporting sustainable development (Syarifullah et al., 2022). Other than the obvious benefit of safety, keeping humans and the environment safe can also improve sustainability outcomes (Nawaz et al., 2019). On the other side, sustainability operationalization, attempting to achieve a balance between economic growth, social development, and environmental protection, is hard to comprehend. The EC framework, in this scenario, may provide

guidance in opening new possible paths for safety and sustainability research. Tools, methods and techniques should be developed to help industries identify the issues with their current production processes and to establish specific measures of progress along with the direction of the sustainable production (Swarnakar et al., 2021; Mech et al., 2022).

Overall, sustainability cannot be as an add-on in the chemical risk assessment, the EC framework dictates that sustainability becomes a way of thinking. The concept of SSbD should be comprehensively understood as an approach to risk analysis or risk assessment, implying that risks for human health, society, and the environment are already assessed in the design phase; a specific risk management strategy; i.e., addressing safety and sustainability by design measures, or by built-in safety and sustainability; or as a result of the design process implying absolute safety and sustainability when the technology is implemented.

An integrated evaluation of safety, functionality and sustainability at any innovation stage should be pursued so that any critical issue could be addressed early enough into the process. In this context, aligning corporate SSbD decision making process to the Agile Stage-Gate innovation model may represent a possible strategy to facilitate the SSbD operationalization (Hristozov et al., 2023; Pizzol et al., 2023). In such an industrial model, the innovation process is divided into five stages: scoping, business case, technical design, testing and validation, and launch. SSbD analysis at each step can inform decisions that may include: termination, whether the technical or commercial probability of success are compromised, or if unacceptable environmental, health and safety risks have emerged; reiteration of the stage, with the aim to improve the safety, performance and/or sustainability of the chemical or product being developed; progression to the next stage if the above mentioned parameters fill in the desired ranges. According to this approach, safer, functional and more sustainable chemicals can be cost-efficiently developed (Hristozov et al., 2023; Pizzol et al., 2023).

Concerning the fields of the SSbD application in the case studies, different settings, including food contact materials, information and communication technologies, cosmetics, and others have been reported, implying that several chemicals/materials have been addressed in the use case/case studies. This large operationalization scenario requires joint and specifically tailored actions focused on promoting the framework application in setting-oriented national research and innovation programmes when developing chemicals and materials. Increasing the availability of findable, accessible, interoperable, reusable (FAIR) data

for SSbD assessment should be pursued to support such aims (Wilkinson et al., 2016). In this context, industry, research and technology organizations as well as the academia should strongly support the improvement of assessment methods, models and tools in a concerted manner. Stakeholders' feedback on different actions should be carefully considered in an iterative, and improvement-oriented process. The development of professional training and educational curricula on skills related to safety and sustainability of chemicals and materials should be also encouraged. In this view, the strength of our pilot study, although certainly constrained by the limited number of retrieved responses, relies on the provided picture on "SSbD culture and operationalization" among the PARC partners, who primarily engaged in chemical risk assessment and management with different expertise. The retrieved results underline the need to promote, inside and outside PARC, the development of relevant scientific knowledge on SSbD, effective trans-disciplinary alignment and optimal use of research data and tools for SSbD to facilitate its effective application into policy, standards and regulation, keeping pace with innovation (Hristozov et al., 2023). This also points out the relevance for risk governance actors to be aware of a SSbD framework that may represent a rigorous, reproducible, and transparent methodology for a comparative assessment of chemicals in terms of safety and sustainability criteria and indicators. This is important to support a suitable dialogue and knowledge sharing between innovators, regulators, producers, downstream users and other stakeholders along all the value chain to ensure the SSbD assessment for chemicals before entering the market and prompt governance actions.

The SSbD framework provides the necessary building blocks and opportunities for new products and is a necessary step in the direction of sustainability, protecting human health and the environment, and ensuring that we operate within the planetary boundaries. Overall, the practical SSbD operationalization will be useful to support the ongoing policy transition towards a prevention-risk governance of chemicals, materials and processes.

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CRediT authorship contribution statement

Veruscka Leso: Conceptualization, Methodology, Data curation, Writing – original draft, Writing – review & editing. **Tomas Rydberd:** Conceptualization, Methodology, Data curation, Writing – original draft, Writing – review & editing. **Maja Halling:** Conceptualization, Writing – original draft, Writing – review & editing. **Spyros Karakitsios:** Writing – review & editing; **Fotini Nikiforou:** Writing – review & editing; **Achilleas Karakoltzidis:** Writing – review & editing. **Denis A. Sarigiannis:** Conceptualization, Writing – review & editing, Supervision. **Ivo Iavicoli:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Supervision.

Declaration of Competing Interest

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

Data Availability

Data will be made available on request.

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References

- Caldeira, C., Farcal, R., Garmendia Aguirre, I., Mancini, L., Tosches, D., Amelio, A., Rasmussen, K., Rauscher, H., Riego Sintes, J., Sala, S., 2022a. Safe and Sustainable by Design Chemicals and Materials - Framework for the Definition of Criteria and Evaluation Procedure for Chemicals and Materials, EUR 31100 EN. Publications Office of the European Union, Luxembourg. ISBN 978-92-76-53264-4, doi:10.2760/487955, JRC128591.
- Caldeira, C., Farcal, R., Moretti, C., Mancini, L., Rasmussen, K., Rauscher, H., Riego Sintes, J., Sala, S., 2022b. Safe and Sustainable by Design Chemicals and Materials - Review of Safety and Sustainability Dimensions, Aspects, Methods, Indicators, and tools. EUR 30991 EN. Publications Office of the European Union, Luxembourg. ISBN 978-92-76-47560-6, doi:10.2760/879069, JRC127109.
- Caldeira, C., Garmendia Aguirre, I., Tosches, D., Mancini, L., Abbate, E., Farcal, R., Lipsa, D., Rasmussen, K., Rauscher, H., Riego Sintes, J., Sala, S., 2023. Publications Office of the European Union. Safe and Sustainable by Design Chemicals and Materials - Application of the SsbD Framework to Case Studies. JRC131878, Luxembourg. <https://doi.org/10.2760/329423>.
- van de Poel, I., Robaey, Z., 2017. Safe-by-design: from safety to responsibility. *Nanoethics* 11 (3), 297–306. <https://doi.org/10.1007/s11569-017-0301-x>.
- EC, European Commission, 2020b. EU Taxonomy for Sustainable Activities. Finance Managed by Directorate-general for Financial Stability, Financial Services and Capital Markets Union. <https://finance.ec.europa.eu/sustainable-finance/tools-and-standards/eu-taxonomy-sustainable-activities.en>. Accessed on 20 June 2024. <https://finance.ec.europa.eu/sustainable-finance/tools-and-standards/eu-taxonomy-sustainable-activities.en>. Accessed on 20 June 2024.
- EC, European Commission, 2020c. Sustain. Prod. Initiat. Law <https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12567-Sustainable-products-initiative.en>. Accessed on 13 May 2024.
- EC, European Commission. Communication from the Commission to the European Parliament, the European Council, the Council, the European Economic and Social Committee and the Committee of the Regions. Chemicals Strategy for Sustainability Towards a Toxic-Free Environment. Com (2020) 667 final. 2020a. Available at <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COMP%3A2020%3A667%3AFIN>. Accessed on 20 June 2024.
- EC, European Commission. Commission Recommendation of 8.12.2022 Establishing A European Assessment Framework for 'Safe and Sustainable by Design' Chemicals and Materials. C(2022) 8854 final. 2022a. Available at <https://research-and-innovation.ec.europa.eu/system/files/2022-12/Commission%20recommendation%20-%20establishing%20a%20European%20assessment%20framework%20for%20safe%20and%20sustainable%20by%20design.PDF>. Accessed on 20 June 2024.
- EC, European Commission. Communication from the Commission to the European Parliament, the European Council, the Council, the European Economic and Social Committee and the Committee of the Regions. The European Green Deal. COM (2019) 640 final. 2019. Available at <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COMP%3A2019%3A640%3AFIN>. Accessed on 20 June 2024.
- EC, European Commission. Corporate Sustainability Reporting. Finance Managed by Directorate-general for Financial Stability, Financial Services and Capital Markets Union. 2023. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32022L2464>. Accessed on 20 June 2024.
- ECHA, 2024. Understanding REACH, 2020. Available online at <https://echa.europa.eu/it/regulations/reach/understanding-reach>. Accessed on May 13. European Chemicals Agency.
- European Commission, 2022b. Directorate-General for Research and Innovation, Safe and Sustainable by Design Chemicals and Materials – A European Assessment Framework. Publications Office of the European Union. Available at <https://data.europa.eu/doi/10.2777/86120>. Accessed on 20 June 2024.
- Hristozov, D., Zabeo, A., Soeteman-Hernandez, L.G., Pizzol, L., Stoychevad, S., 2023. Safe-and-sustainable-by-design chemicals and advanced materials: a paradigm shift towards prevention-based risk governance is needed. *RSC Sustain.* 1, 838–846. <https://doi.org/10.1039/d3su00045a>.
- Marx-Stoelting, P., Riviere, G., Luijten, M., Aiello-Holden, K., Bandow, N., Baken, K., Cañas, A., Castano, A., Denys, S., Fillol, C., Herzler, M., Iavicoli, I., Karakitsios, S., Klanova, J., Kolossa-Gehring, M., Koutsodimou, A., Vicente, J.L., Lynch, I., Namorado, S., Norager, S., Pittman, A., Rotter, S., Sarigiannis, D., Silva, M.J., Theunis, J., Tralau, T., Uhl, M., van Klaveren, J., Wendt-Rasch, L., Westerholm, E., Rousselle, C., Sanders, P., 2023. A walk in the PARC: developing and implementing 21st century chemical risk assessment in Europe. *Arch. Toxicol.* 97, 893–908. <https://doi.org/10.1007/s00204-022-03435-7>.

- Mech, A., Gottardo, S., Amenta, V., Amodio, A., Belz, S., Bøwadt, S., Drbohlavová, J., Farcál, L., Jantunen, P., Malyska, A., Rasmussen, K., Riego Sintes, J., Rauscher, H., 2022. Safe- and sustainable-by-design: the case of smart nanomaterials. a perspective based on a European workshop. *Regul. Toxicol. Pharmacol.* 128, 105093. <https://doi.org/10.1016/j.yrtph.2021.105093>.
- Nawaz, W., Linke, P., Koç, M., 2019. Safety and sustainability nexus: a review and appraisal. *J. Clean. Prod.* 216, 74–87. <https://doi.org/10.1016/j.jclepro.2019.01.167>.
- OECD, 2020. Moving Towards a Safe(r) Innovation Approach (SIA) for More Sustainable Nanomaterials and Nano-enabled Products. Series on the Safety of Manufactured Nanomaterials. Available at <https://www.oecd.org/chemicalsafety/safer-and-sustainable-innovation-approach/>. Accessed on 20 June 2024. Available at <https://www.oecd.org/chemicalsafety/safer-and-sustainable-innovation-approach/>. Accessed on 20 June 2024.
- Pizzol, L., Livieri, A., Salieri, B., Farcál, L., Soeteman-Hernández, L.G., Rauscher, H., Zabeo, A., Blosi, M., Costa, A.L., Peijnenburg, W., Stoycheva, S., Hunt, N., López-Tendero, M.J., Salgado, C., Reinoso, J.J., Fernández, J.F., Hristozov, D., 2023. Screening level approach to support companies in making safe and sustainable by design decisions at the early stages of innovation. *Clean. Environ. Syst.* 10, 100132. <https://doi.org/10.1016/j.cesys.2023.100132>.
- Sudheshwar, A., Apel, C., Kümmerer, K., Wang, Z., Soeteman-Hernández, L.G., Valsami-Jones, E., Som, C., Nowack, B., 2024 Jan. Learning from safe-by-design for safe-and-sustainable-by-design: mapping the current landscape of safe-by-design reviews, case studies, and frameworks. *Environ. Int.* 183, 108305. <https://doi.org/10.1016/j.envint.2023.108305>. Epub 2023 Nov 4. PMID: 38048736.
- Swarnakar, V., Singh, A.R., Antony, J., Tiwari, A.K., Cudney, E., 2021. Development of a conceptual method for sustainability assessment in manufacturing. *Comput. Ind. Eng.* 158, 107403. <https://doi.org/10.1016/j.cie.2021.107403>.
- Syaifulah, D.H., Tjahjono, B., McIlhatton, D., Zagloel, T.Y.M., 2022. The impacts of safety on sustainable production performance in the chemical industry: a systematic review of literature and conceptual framework. *J. Clean. Prod.* 366, 132876. <https://doi.org/10.1016/j.jclepro.2022.132876>.
- Wilkinson, M.D., Dumontier, M., Aalbersberg, I.J., Appleton, G., Axton, M., Baak, A., Blomberg, N., Boiten, J.W., da Silva Santos, L.B., Bourne, P.E., Bouwman, J., Brookes, A.J., Clark, T., Crosas, M., Dillo, I., Dumon, O., Edmunds, S., Evelo, C.T., Finkers, R., Gonzalez-Beltran, A., Gray, A.J., Groth, P., Goble, C., Grethe, J.S., Heringa, J., 't Hoen P.A., Hooft, R., Kuhn, T., Kok, R., Kok, J., Lusher, S.J., Martone, M.E., Mons, A., Packer, A.L., Persson, B., Rocca-Serra, P., Roos, M., van Schaik, R., Sansone, S.A., Schultes, E., Sengstag, T., Slater, T., Strawn, G., Swertz, M. A., Thompson, M., van der Lei, J., van Mulligen, E., Velterop, J., Waagmeester, A., Wittenburg, P., Wolstencroft, K., Zhao, J., Mons, B., 2016. The FAIR guiding principles for scientific data management and stewardship. *Sci. Data* 3, 160018. <https://doi.org/10.1038/sdata.2016.18>.