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Avoiding tomorrow's chemical mistakes today

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The Safe and Sustainable by Design (SSbD) framework is gaining momentum within the European Union, with scholars, industry, and policymakers actively testing its application. This Perspective highlights the central challenges that remain, particularly in relation to methods and data. The current methodological pillars of SSbD, Hazard Assessment (HA), Risk Assessment (RA), and Life Cycle Assessment (LCA) provide a solid basis for evaluating chemical safety and sustainability, as well as identifying potential trade-offs. Yet their integration with design, innovation, and broader ethical and social considerations remains underdeveloped. Beyond these methodological gaps, the greatest obstacle to SSbD is the availability and quality of data. Despite substantial progress in advancing safety and sustainability assessments, improvements in data generation, accessibility, and reliability have lagged far behind. Since both safety and sustainability evaluations depend critically on data, this imbalance undermines the framework's effectiveness. We propose a three-step data strategy focused on safety data as a starting point. Advancing SSbD in a meaningful way requires a robust, regulatory-based approach to improve data availability and quality for both safety assessments and LCA. Without such a strategy, further methodological innovation risks becoming an empty exercise that obscures rather than advances real progress.

Green foundation

1. The Safe and Sustainable by Design (SSbD) framework is rapidly advancing across the European Union, with researchers, industry, and policymakers actively testing its implementation. We highlight key challenges that persist, especially around methods and data.
2. SSbD's core pillars, Hazard Assessment (HA), Risk Assessment (RA), and Life Cycle Assessment (LCA), offer a robust foundation for evaluating chemical safety and sustainability while revealing critical trade-offs. Yet their integration with design, innovation, and broader ethical and social dimensions remains limited. Above all, insufficient and inconsistent data present the most significant barrier to progress.
3. Although methods for assessing safety and sustainability have matured, data generation, accessibility, and reliability lag behind. Because SSbD depends on trustworthy data, this gap threatens its credibility. We propose a targeted three-step data strategy to ensure SSbD evolves into a transformative, evidence-driven framework.

The triple planetary crisis, climate change, biodiversity loss, and pollution, is putting global well-being at risk. Human pressure on 'climate change', 'biosphere integrity', 'land system change', 'freshwater use', 'biogeochemical flows', and 'novel entities' transgresses the planet's capacity, also known as the Earth's planetary boundaries.[1] The planetary boundary for 'novel entities' refers to the boundary of truly novel anthropogenic introductions to the Earth system, including synthetic chemicals, nanomaterials, plastics, and genetically modified organisms.[2] The annual production of novel entities and newly synthesized chemicals outpaces safety evaluations. At the same time, monitoring covers only a small fraction of the chemicals and materials produced, while the chemical pressure on biosphere integrity already transgresses its planetary boundary.[2] We discuss emerging policies addressing chemical pressure and their methodological challenges, with a focus on the importance of advancing open and reliable data.

History has repeatedly shown that we often fail to anticipate the full consequences of our technological advances, leading to ineffective solutions and potential "regrettable substitutions" with potentially devastating outcomes. For example, the use of Softenon (Thalidomide) as a tranquilizer for pregnant women tragically caused birth defects. Similarly, many chemical substitutions intended to mitigate harm have resulted in "regrettable solutions" due to insufficient early risk assessments or a lack of regulatory action, even when risks were known. For instance, chemical manufacturers substituted bisphenol A (BPA) with bisphenol B (BPB) in baby bottles and food packaging, despite evidence of similar health concerns.[3]

Likewise, case-by-case PFAS (also known as 'forever chemicals') regulation perpetuates a system of "regrettable substitutions" in which regulated compounds are replaced with

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unregulated and understudied alternatives. An example is GenX being a common replacement for PFOA (a PFAS member), which has been found to have similar toxicological profiles and higher environmental mobility.[4] Additionally, newer insecticide groups such as neonicotinoids,[5] initially introduced as biodegradable and highly specific alternatives to broad-spectrum and persistent chemicals like DDT and organophosphates, ended up causing greater harm than anticipated to a wide range of non-target organisms and disrupted entire ecological networks. Chemical substitution can sometimes mean replacing one type of hazard with another. For instance, hydrochlorofluorocarbons (HCFCs) and hydrofluorocarbons (HFCs) were widely used as non-flammable cooling agents in refrigeration systems. They have largely been replaced by hydrofluoroolefins (HFOs), which have a much lower global warming potential and therefore reduce environmental impact. However, HFOs are mildly flammable, shifting the primary concern from climate effects to fire and explosion risks. This transition necessitates new safety measures for their handling and storage.[6]

These are prime examples of "wicked problems": complex, multifaceted challenges marked by competing priorities, deep uncertainties, and the absence of clear-cut solutions. Tackling such challenges demands a paradigm shift: a steadfast commitment to proactive, science-based, and ethically grounded approaches to innovation and risk management. It also requires a deliberate effort to learn from past mistakes to ensure they are not repeated.

In response to these pressing challenges, the European Commission published an assessment framework for 'safe and sustainable by design' chemicals and materials in 2022.[7] This forward-thinking, pre-market approach focuses on developing chemicals that deliver essential functionality[8] while avoiding harmful properties and excessive volumes that endanger human health and the environment. SSbD emphasizes sustainability throughout a chemical's lifecycle by minimizing its environmental footprint, including impacts on climate change, resource consumption, ecosystems, and biodiversity. At the core of the Safe and Sustainable by Design (SSbD) approach is the imperative to screen and benchmark all chemicals for safety and sustainability before they reach the market. This is especially critical given the staggering reality that, *e.g.*, under the EU's REACH regulation (Registration, Evaluation, Authorisation, and Restriction of Chemicals) no more than 4400 decisions were made related to 15 000 submissions covering more than 2900 substances between 2009–2024,[9] and under the U.S. EPA's Toxic Substances Control Act (TSCA) no more than 38 existing chemicals[10] have been formally evaluated since 1979 and all new chemicals (approximately 400–500 each year)[11] have undergone a 'pre-manufacture review' since 2016 from a total of about 86 000 substances registered[12] as of 2025, despite an estimated 40 000–350 000 chemicals[13,14] currently in commercial use and production.

Key methods supporting the SSbD framework currently include Hazard Assessment (HA), Risk Assessment (RA), and Life Cycle Assessment (LCA).[15,16] While these methods provide a strong foundation for evaluating chemical safety and sustainability, as well as mapping possible trade-offs between them, the integration with design, innovation, and ethical and social considerations remains a critical gap, largely overlooked and underdeveloped. However, in the absence of integration with innovation-oriented approaches, opportunities to reformulate the solution to achieve both reduced toxicity and diminished environmental impact may be overlooked. Ethical considerations are seldom systematically incorporated into these assessment frameworks. Examples include the exclusion of raw materials associated with human rights violations or the often unequal distribution of pollution threats, with marginalized and low-income communities facing higher exposure and receiving less protection. Similarly, social dimensions, such as societal acceptance of novel manufacturing processes, remain largely unaddressed within current SSbD implementations.

Moreover, the transition to a circular economy (CE) underscores the need for a fundamental shift in how we manage materials and chemicals. A CE aims to eliminate waste, recycle products, conserve resources, and reduce emissions.[17] However, one of its major challenges is the presence of contaminations of hazardous substances in products, which can be transferred into waste streams and reintroduced through recycling. These chemicals of concern can undermine efforts to establish a circular economy.[18] Finally, in the European Commission's definition of SSbD above, the life cycle of the chemical is key for assessing the sustainability component. However, substituting a chemical of concern in a product with an alternative can also affect the product's durability, performance, and material integrity. These trade-offs underscore the importance of considering the entire product life cycle, not just the chemical or material life cycles.[19] Addressing these challenges is essential for ensuring that SSbD evolves into a truly systemic and global approach, capable of driving responsible and transformative innovation.

Besides these purely methodological challenges, the biggest obstacle for Safe and Sustainable by Design (SSbD) studies is data, both in terms of availability and quality. SSbD faces a dual data challenge: reliable information is lacking for both chemical safety assessments and LCA. These challenges differ in nature. In safety assessments, data for newly developed chemicals are prospectively estimated with large uncertainties, while data for many existing chemicals, though more abundant and verified with observations, is often incomplete, inconsistent, or contains contradictory findings with limited or no interpretation. For LCA, relevant data often exists within companies but is rarely shared publicly. In both cases, the available data may be incomplete and of uncertain quality. Since the results of these assessments depend on the data they rely on, the quality and transparency of input data are crucial. Currently, industry remains the primary source of much of this data. However, voluntary data sharing is still limited, mainly due to the lack of a global level playing field and concerns about competitiveness.

In the meantime, researchers are investigating whether technologies like artificial intelligence (AI) and machine learning (ML) can help bridge data gaps. However, these tools depend on tailored and high-quality training data, which is often lacking, as we have just observed. Moreover, public LCA databases, for example, are frequently outdated or incomplete. Training models or generating new datasets based on such sources, especially through web scraping without properly accounting for differences regarding system boundaries and definitions, can lead to serious distortions.

To advance SSbD in a meaningful way, targeted regulatory measures are indispensable, not just to improve data availability for safety assessments and LCA but also to ensure its quality, transparency, and relevance. Ideally, applying the precautionary principle, full and peer-reviewed chemical and LCA data sets would be collected before substances are allowed on the market. However, given the vast number of chemicals and the time required to gather and review complete data, this approach is impractical. Alternatively, relying solely on post-market testing presents similar challenges and essentially maintains the current, inadequate system.[20]

A more effective approach would combine the strengths of both strategies (Fig. 1). One option is to first screen all chemicals, new and existing, for inherent toxicity and persistence (either or not combined with bioaccumulation as Persistent, Bioaccumulative, and Toxic (PBT) approach outlined in REACH Annex XIII), develop clear and consistent rules, and enforce them within and at the borders of major economic markets. While this first step, which is currently implemented in the EU, could help block the next generation of PFAS-like 'forever chemicals' and will not need LCA data collection, it won't address the broader accumulation of smaller-scale chemical impacts. A second step is therefore needed: collecting additional data on other substances. This should be guided by clear criteria that specify the minimum data requirements, while remaining as consistent as possible with existing practices. To increase the practicability of this second step, data requirements should be kept to a minimum, complemented by field-based monitoring systems that are better suited to capture real-world risks (the so-called lab-field extrapolation in all its dimensions).[21] For this step, the division of roles between government and industry should be that responsibility for data collection lies with the industry that introduces new chemicals, while interpretation and field monitoring are the responsibility of the government, thereby ensuring independence. Data quality as one aspect of 'interpretation' could be checked and assured by establishing this step by acknowledged international organizations such as the OECD, building

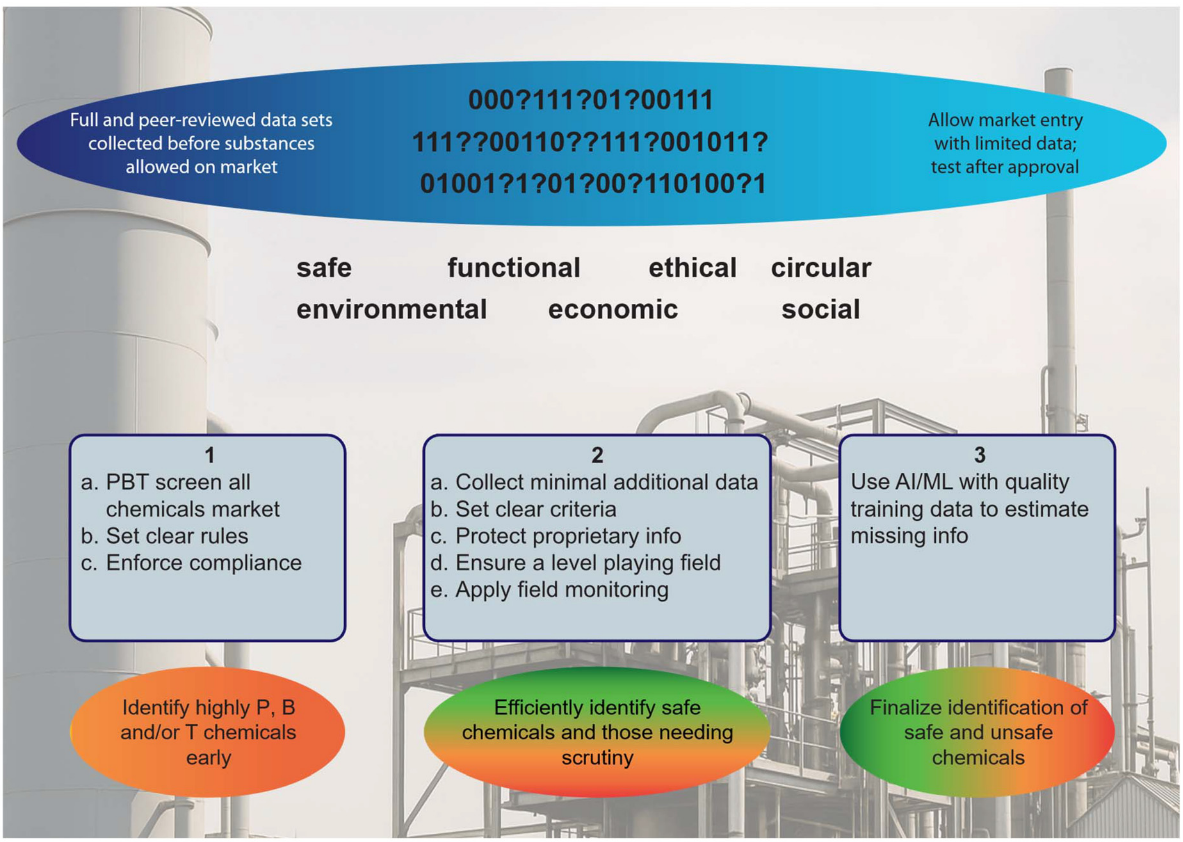

Fig. 1 A three-step data strategy for SSbD with a focus on safety data. To advance SSbD in a meaningful way, an effective and efficient regulatory-based data strategy is required to improve data availability and quality for safety assessments and LCA. If we fail to effectively and efficiently address this issue but continue to introduce new methodological concepts, we are merely beating around the bush and fooling ourselves with false promises.

upon their recently published Guidance document for regulatory assessments.[22] It should also address how proprietary information ("chef's secrets") can be protected, such as through blockchain-based tools or limited disclosure mechanisms, and define how to ensure a level playing field, ideally through global coordination or cooperation among major economic blocs. The more countries and continents adopt such regulation, the more effective it will be, yet recent failures, such as the breakdown of negotiations on a UN plastics treaty, illustrate how difficult this global alignment currently is. Once a sufficiently robust dataset is established, a third step could involve applying New Alternative Methodologies (NAMs)[23] and Artificial Intelligence (AI).[24–26] For example, NAMs and Artificial Intelligence (AI) can be used to estimate and extrapolate missing information, this time, drawing on higher-quality training sets, increasing reliability. While this strategy primarily addresses safety data, applying SSbD, for example, in substituting currently used hazardous substances, will also require scarce LCA data. Improving the availability and quality of such data will demand incentives, through regulation and enforcement, for industries to publish relevant datasets. These regulations should simultaneously safeguard proprietary information, ensure a level playing field, and in doing so help generate stronger training data for the subsequent application of AI, which is also beginning to emerge in the context of LCA.[27,28]

Finally, as part of this data strategy, the scientific community should place particular emphasis on several key areas, including (but not limited to) advancing new approach methodologies (NAMs) for data estimation;[23] strengthening trust as a critical factor for the regulatory acceptance of AI models;[29] and improving approaches to address chemical mixtures, the vast number of which, along with their synergistic or cumulative effects, cannot yet be fully characterized or predicted. Mixture assessment factors to account for the elevated risks posed by chemical mixtures[30] are incorporated pragmatically within RA, addressing uncertainties in mixture effect predictions that are inherently difficult to assess.

The authors of this article have been in the field for nearly or over 30 years. During that time, significant methodological progress has been made in both safety and sustainability assessments. However, progress on data availability and quality has been far slower and more uneven, even though both safety and sustainability assessments rely heavily on these data. If we fail to effectively and efficiently address this issue but continue to introduce new methodological concepts, we are merely beating around the bush and fooling ourselves with false promises.

Author contributions

Conceptualization: J. B. G., M. G. V.; methodology: J. B. G., M. G. V.; visualization: J. B. G., M. G. V.; writing – original draft: J. B. G; writing – review & editing: M. G. V.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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