Environmental Science Nano

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Cite this: *Environ. Sci.: Nano*, 2025, 12, 4008

The SAbyNA platform: a guidance tool to support industry in the implementation of safe- and sustainable-by-design concepts for nanomaterials, processes and nano-enabled products†

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Simple, cost-effective and reliable methods are needed for pragmatic, flexible, safe and sustainable evaluations at early stages of product (chemical/material) development. This is especially true for nanoforms and nano-enabled products, for which guidance on the application of validated methods and tools for the assessment and management of safety and sustainability is still lacking. The SAbyNA guidance platform fills these gaps in the following ways: by integrating i) informative modules covering the needs of all stakeholder profiles (*i.e.*, industry, consultants, RTOs, and regulatory bodies) by guiding them in the choice of methods, models and tools for exposure and hazard assessment, as well as in the selection of specific safe-by-design interventions; and ii) assessment modules for a screening-level evaluation of environmental sustainability and costs and for a screening and detailed safety assessment of nanoforms and nano-enabled products along their life cycle. The potential of this digital tool to support different stakeholders towards safer and more sustainable developments is demonstrated in a real case study: a nano-enabled 3D-printed vacuum cleaner plastic component composed of single-walled carbon nanotube–polycarbonate composites with antistatic properties. This study shows how a user inputs data to perform a screening assessment on an additive manufacturing case study, and the digital platform provides the user with some safe-by-design recommendations, such as reducing the fiber length or rigidity or changing process parameters to reduce emissions. Hazard, exposure, costs, sustainability and functionality case study data were added in the detailed assessment module of the platform to check whether the implemented safe-by-design intervention was able to improve the safety profile of this nano-enabled product without affecting sustainability and functionality performances. This study also demonstrated the added value of using the SAbyNA guidance platform at the early stage of the nano-enabled product development for the quantification and visualization of safety, sustainability, cost and functionality aspects of nano-enabled products and processes.

Received 20th March 2025,
Accepted 16th June 2025

DOI: 10.1039/d5en00312a

rsc.li/es-nano

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† Electronic supplementary information (ESI) available. See DOI: https://doi.org/10.1039/d5en00312a

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Environmental significance

Recent European agreements (*e.g.*, the European Chemicals Strategy for Sustainability and the Zero Pollution Action Plan) incentivise the transition towards climate neutrality and a toxicity-free environment. This can be achieved through the combined safety and sustainability assessments of chemicals/materials. Therefore, a tool supporting different stakeholders towards safer and more sustainable developments is needed, especially for nanoforms and nano-enabled products, as validated methods and tools for the safety and sustainability assessment of nanomaterials are still lacking. The SAbyNA platform presented in this article integrates in a single tool the assessment of human and environmental safety, costs and sustainability aspects and the suggestion of appropriate strategies to reduce or mitigate risks from nanoforms and nano-enabled products along their life cycles.

Introduction

Recent European agreements such as the European Green Deal,[1] the European Chemicals Strategy for Sustainability (EC-CSS)[2] and the Zero Pollution Action Plan[3] incentivise the transition towards climate neutrality and a toxicity-free environment.

In this context, the European Commission (EC) Joint Research Centre (JRC) developed a Safe and Sustainable by Design (SSbD) framework to support the design and development of safe and sustainable chemicals and materials through research and innovation activities. In the last few years, the EC-JRC has published several reports on SSbD, including the SSbD framework for the definition of criteria and evaluation procedure for chemicals;[4] a review of safety and sustainability dimensions, aspects, methods, indicators and tools;[5] the application of the SSbD framework to case studies[6] and an updated SSbD methodological guidance with the first round of feedback from stakeholders.[7] The SSbD framework focuses on the early stages of the product innovation process to provide chemicals, materials and products that fit into circular economy models while minimising harmful properties and negative impacts on human health and the environment during their life cycle. However, the application of SSbD in real production contexts is still a key point for the refinement of the framework, as guidance on how and when to apply existing methodologies and assessment tools is needed for pragmatic and flexible SSbD implementation.[8] Moreover, additional efforts are needed when the framework is applied to emerging materials, such as nanoforms (NFs) and nano-enabled products (NEPs), since safety and sustainability data for these substances are still missing, and assessment methods and tools are yet not fully validated for these materials in all the life cycle stages as they are for not-nano materials.

In this regard, the EU H2020 SAbyNA project aimed to provide guidance on how and when to use existing (distilled and streamlined) key resources (*i.e.*, methods, models, tools and guidelines) to implement the SSbD framework for NFs and NEPs *via* a user-friendly digital guidance platform (**https://platform.sabyna.eu/**). The SAbyNA guidance platform consists of optimised workflows to support the development of safe-by-design (SbD) NFs, NEPs and processes over their whole life cycle while considering functional performance and environmental sustainability. The adapted SbD strategies accessible *via* the SAbyNA guidance platform aim to maximize human and environmental safety as well as selected sustainability features while retaining the functionality provided by the use of nanotechnologies.

The SAbyNA platform uses existing resources that could be either reimplemented into the platform or adapted to the purpose of SSbD. The key resources reused are the GUIDEnano risk assessment tool (**https://tool.guidenano.eu/**) developed in the FP7 GUIDEnano project (G.A. 604387) and the GRACIOUS blueprint (**https://doi.org/10.5281/zenodo.549761**) from the GRACIOUS H2020 project (G.A. 760840).

In addition, the project collected the needs and concerns of relevant stakeholders (*i.e.*, industry, consultants, RTOs, and regulatory bodies) on how to implement SSbD through an initial questionnaire and then through workshops to evaluate whether the platform could fulfil their expectations. Stakeholder feedback was considered by the developers of the digital guidance platform, which led to modifications in specific sections of the platform (*e.g.*, the integration of informative modules in the platform to guide the user in performing hazard/exposure assessment or in the selection of SbD interventions to mitigate potential risks).

The present study describes the different modules of the SAbyNA platform and how this digital guidance can help industrial users in the field of nanotechnology implement SSbD principles in their innovation process. This platform is a result of multidisciplinary collaboration between experts: (eco)toxicologists, materials scientists, risk assessors, social psychologists, and modelling developers. In addition, testing and refinement through industry consultation reinforced the relevance and applicability of the guidance platform to implement SSbD concepts, as demonstrated by real industrial case studies. This study also provides the first insights into how all the steps of the JRC framework, except for step 5 on socio-economic sustainability assessment, could be implemented using the SAbyNA Platform.

The usability of the different modules of the platform is illustrated through a real case study, reflecting one of the two important sectors for which SAbyNA provides focused strategies grounded in collaboration with industrial experts: the additive manufacturing sector. This case study investigated an SSbD solution to obtain a safer and more sustainable nano-enabled 3D-printed vacuum cleaner component with antistatic properties, composed of a polycarbonate (PC) matrix and single-walled carbon nanotubes (SWCNTs).

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The SAbyNA platform

The SAbyNA platform is developed to support the needs of all stakeholders, especially selecting the optimal pathway (and associated resources) to identify safety concerns posed by NFs, NEPs and processes. In addition, appropriate strategies are identified to reduce or mitigate those concerns and to improve sustainability performance using existing data, methods, models and tools. To meet these goals, the SAbyNA platform consists of six modules with two purposes: first, informing, explaining and guiding the choice of these science-based resources; second, facilitating their direct application to conduct safety and sustainability and cost assessments.

Informative modules

Four informative modules (1) exposure and hazard assessment guidance, 2) SbD interventions towards safer products, 3) SbD interventions towards safer processes, and 4) database resources) provide all the necessary information to the user on the methods, models and tools more suitable for exposure and hazard assessment, and on SbD interventions and how to apply them to reduce/mitigate identified risks associated with the NF, NEP or process (Fig. 1).

Furthermore, there is a module providing a connection with the database resources available in the area of nanosafety for use in the assessment section.

Exposure and hazard assessment guidance

In this module, guidance has been developed to help users with exposure and hazard assessment.

The release and exposure assessment strategy includes models, tools and methods to assess the release and exposure of NFs and NEPs to workers, consumers and the environment. The identification and selection of these models/tools for NFs and NEPs followed a well-defined methodology deeply explained and publicly available based on Hanlon *et al.* 2021.[9] In this section of the platform, the user is guided through the selection of the model or tool that fits with the objective of the analysis (workers, environmental, and consumer exposure assessment), considering their level of expertise in release and exposure assessment (*e.g.*, beginner, advanced, and expert) and considering whether the model/tool is nano-specific or not. Additionally, the user can find existing guidance and technical documents available from the European Chemicals Agency (ECHA), the Organisation for Economic Co-operation and Development (OECD) and the International Standardization Organization (ISO) to assess the release of NFs and potential exposure to workers, consumers and the environment. These guidance/protocols were also used in the safety assessment section of the platform to guide the user in classifying the assessed NEP based on indications provided in the guidelines, which are not only nano-specific, *e.g.*, for consumers' exposure,[10] and for workers' exposure.[11] Although

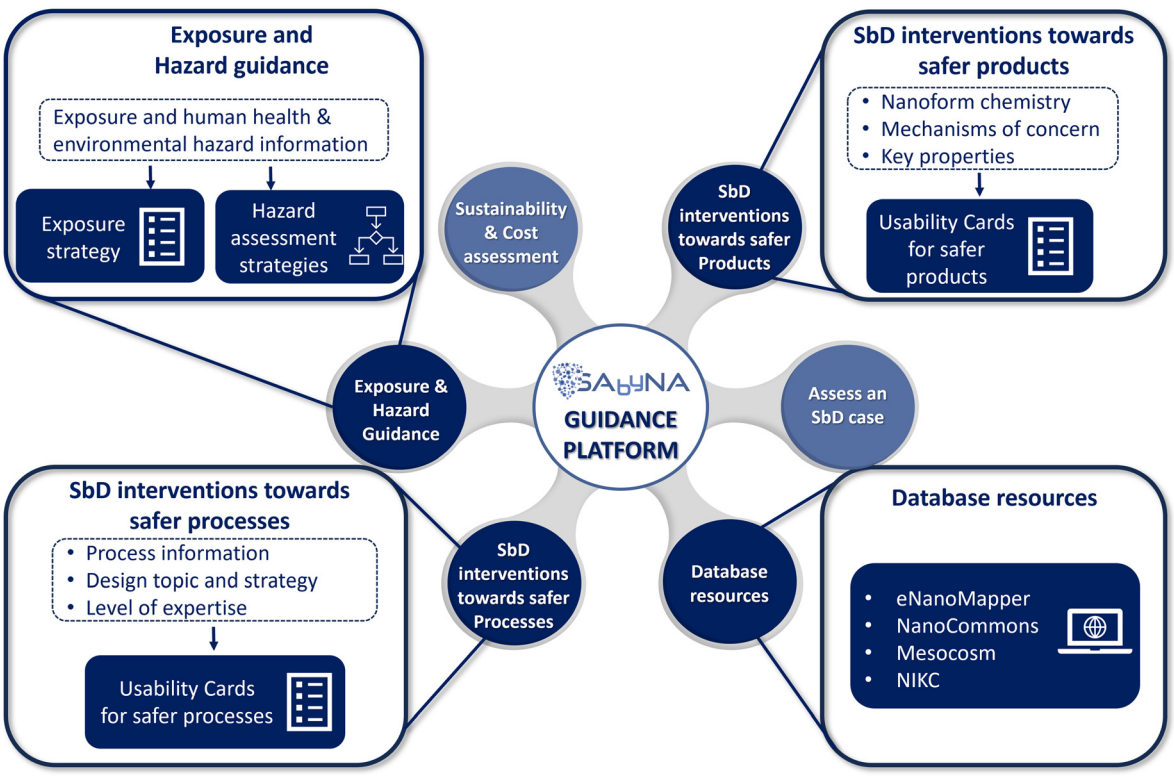

Fig. 1 General structure and main contents of the four informative modules of the SAbyNA platform.

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a technical report developed by ISO was published in 2021 to help evaluate methods for assessing the release of nanomaterials from commercial nanomaterial-containing polymer composites,[12] the complex assessment of NFs released from NEPs does not yet benefit from a standardised approach, such as an ISO TS. Therefore, to facilitate the release assessment, SAbyNA partners in collaboration with the OECD are preparing a guidance document for the selection of the most appropriate release testing considering the different uses of the material/products under assessment, the process/activities leading to potential releases, the system/environmental compartments (receptor) in which the release can end up, and the target population exposed.[13] In the absence of environmental release data, specific environmental release categories (SPERCs) may be used to estimate releases from specific product categories by providing general emission factors and their applicability to specific NEPs (use maps – ECHA).

The SAbyNA hazard assessment guidance provides insight into the scientific foundations and scope of the hazard assessment strategies developed for the two levels of hazard assessment of NF and NEPs included in the platform: screening and detailed assessment. The hazard screening is intended to provide early hazard warnings based on i) physico-chemical features that have been previously identified as potentially hazardous; ii) core chemistry; and iii) known classification labelling and packaging (CLP)-based classification of NFs and bulk materials of the same core chemistry. This screening phase is common to both human health and environmental hazard assessment and does not require any toxicity testing as it is based on existing information about the NF (or core chemistry) under investigation, making it suitable for the earliest design stages before the NF is synthesized. The detailed hazard assessment phase considers the different human and environmental exposure routes and provides specific integrated approaches to testing and assessment (IATAs) for NFs. Human health hazard assessment is based either on existing data and information or on data generated through simple, cost-effective, predictive, and robust *in vitro* assays. Following these IATAs, the user can predict hazard warnings for the most relevant toxicological endpoints common to multiple adverse outcomes: cytotoxicity, oxidative stress, inflammation, and genotoxicity.[14] In addition, the assessment of dissolution provides an estimation of the potential bioaccumulation of the material, which can be used to infer potential toxicity depending on the exposure route.[14] Recommendations on how to deal with the interferences of materials in the assays, and specific adaptations of the assays to NEPs are also provided. The guidance document includes information on the toxicity endpoints considered in the hazard strategy, where and how to gather publicly available data in specialised databases, and how to generate new hazard data in the case of data gaps. Regarding the last point, this guide includes suggestions on the experimental testing to perform how to combine results from different assays into a final endpoint outcome, how to analyse the generated data and which thresholds to apply for each assay to decide whether an NF raises a concern.

The guidance for the detailed environmental hazard assessment step specifies how to establish any indications of environmental hazard for an NF and guides the user on how to generate the evidence required to make decisions regarding what should be the intervention target of any SbD options. This guidance includes how to perform ecotoxicity testing for NFs and, importantly, how to establish normalised effect threshold concentrations for NFs for pairwise comparisons of environmental hazards between NF design options. This can be either from existing data through the construction of species sensitivity distributions, or from targeted testing of new, data-poor NFs. These normalised effect threshold concentrations then serve as hazard indicator inputs to the assessment module of the platform (assess an SbD case). Similar to the human health hazard assessment, guidance is also provided on how to adapt the assessment for NEPs.

SbD interventions towards safer products and safer processes

Effective SbD implementation in real industrial settings calls for usable methods for designing safer NFs that can be manufactured by safe processes.[15]

The minimization of risks arising from using specific NFs can be obtained by applying methods that minimize the hazard of NFs and/or limit or prevent NF release from NEPs (minimizing exposure). Numerous methods have been described in the literature. This platform module includes a curated selection of publications describing only these methods that provide i) a clear goal (targeting the reduction of hazard or reduction/mitigation of emissions/exposure), ii) the potential to be scaled up to industrial volumes, iii) the preservation of the technical function after the modification suggested (SbD intervention), vi) an application of the SbD strategy to different types of NFs, and v) an estimation of costs and benefits. All the details related to the methodology used to select SbD strategies for NFs/NEPs are reported in D4.2 (ref. 16) based on the literature review reported in D4.1.[17]

To deliver this information in a format suitable for the platform, the main characteristics of each selected SbD intervention towards safer NFs/NEPs were summarized and presented as usability cards for the platform users, where the main feature of the SbD intervention is described in at most 15 lines, including.

- NFs to which it has been applied,
- Physico-chemical driver of the hazard,
- Mechanism of concern,
- Method proposed to minimize it,
- Link to the resource information with all the details.

An example of a usability card for safer NEP is reported in ESI† S1. The relationship between the physical–chemical

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transformations of an NF and its toxicological outcomes is described by Delpivo *et al.*[18]

Analogous to the usability cards of SbD interventions for NFs and NEPs, the platform includes usability cards for SbD interventions applied to processes. The cards described and summarized over 150 documents, including standard protocols, models, tools, frameworks, databases, as well as previous outcomes from FP7 and H2020 projects, such as NanoReg2 (G.A. 310584), caLIBRAte (G.A. 686239) and GUIDEnano (G.A. 604387).

The usability cards for safer processes essentially summarise the key components of each resource in a 1–2-page layout that permits their identification using a sorting system for each category, which includes.

- Level of expertise of the user (*i.e.*, expert, advanced, and beginner).
- Design strategy (*e.g.*, emission verification, exposure mitigation measures, inherently safe design, risk assessment, safeguarding and complementary protective measures);
- Design topics (*e.g.*, efficiency, emission of hazardous materials and substances, explosion, and regulatory aspects);
- Type of actions (risk management measures (RMM) and new process design);
- Filter (specific word search/filter).

All the sources used were reported in D5.1,[19] and the selection of the most suitable resources based on applicability, user-friendliness and robustness was presented in D5.2.[20] An example of a usability card for safer processes is also reported in ESI† S1.

Database resources

Links to the different public database resources are available in this module of the platform (*i.e.*, eNanoMapper, NanoCommons, MESOCOSM, and CEINT NIKC), where the user can easily find the physico-chemical characteristics of an NF and release/exposure/hazard data. The eNanoMapper system (**https://enanomapper.adma.ai/**) was developed as part of the EU-sponsored FP7 project (EC G.A: 604134) to establish a community-agreed ontology, database system and modelling platform to support various domains of nanotechnology. To help standardise and harmonise ongoing nano environment health and safety (EHS) research data storage efforts, its use has been promoted as a central database system. The eNanoMapper system has been used as the main data repository for many of the recently completed and currently ongoing nanosafety projects (*e.g.*, NANOGENOTOX, MARINA, NANoREG, Nanoreg2, caLIBRAte, GRACIOUS, PATROLS, SbD4Nano, HARMLESS and Gov4Nano) by remapping data onto an internal data structure based on the GRACIOUS blueprint. The link of the NanoCommons (**https://www.nanocommons.eu/**) is also available in the platform, where the user can find this open accessible e-infrastructure integrating data on physicochemical characterization and interaction mechanism knowledge, protocols and data on NFs. The MESOCOSM database (**https://aliayadi.github.io/MESOCOSM-database/**) is a comprehensive and exclusive database on the environmental exposure and hazard data of NFs obtained in aquatic mesocosms designed by LabEx SERENADE (safe(r) eco-design research and education applied to nanomaterial development).[21,22] This database can be used as a benchmarking source to improve both the safety and efficacy of manufactured NFs, and it is available as a downloadable JSON file for free under Open Database License v1.0. The link to the CEINT NanoInformatics Knowledge Commons (NIKC) (**https://ceint.duke.edu/research/nikc/**) can also be employed by the user to find metadata on nanomaterial transformations in an organizational structure permitting readily accessible data for broader scientific inquiry.[23] The NIKC is a custom cyberinfrastructure consisting of a data repository and associated analytical tools developed to visualize and interrogate integrated datasets.

Assessment modules

Two assessment modules (*i.e.*, sustainability and cost assessment, and Assess an SbD case) offering the opportunity to conduct a screening LCA and cost assessment, and a screening and a detailed safety assessment for NFs and NEPs are included in the platform, respectively. The two assessment modules of the platform and the flows of information/data are shown in Fig. 2. Detailed information on how the safety assessment module of SAbyNA was developed based on the GUIDEnano tool and the GRACIOUS blueprint is provided in ESI† S2. In the sustainability and cost assessment module, a set of LCA and cost assessment-based indicators was selected to be used in a screening assessment for the candidate NF. In the Assess a SbD case module, the platform provides a screening assessment (less data-demanding part) and a more detailed assessment (data-demanding part). In this module of the platform, data inputs are gathered (from databases or user data inputs) and organised through assessment scenarios based on a holistic approach that follows an iterative process of feedback loops, which allows the use of the informative modules in the platform.

Moreover, in the last part of this module, the user can manually add the LCA and cost assessment data to be combined with the safety results to visualise the safety and sustainability outcomes for each assessment scenario.

Sustainability and cost assessment

Within this module, the SAbyNA platform offers the possibility of integrating a case-specific simplified LCA and cost analysis at different levels, from a streamlined evaluation to a more detailed assessment. The module consists of downloadable Excel tools meant to enable the comparative evaluation of up to 5 scenarios.

The proposed simplified LCA intends to support environmental sustainability assessment from the life cycle perspective described in step 4 of the JRC SSbD Framework.[4]

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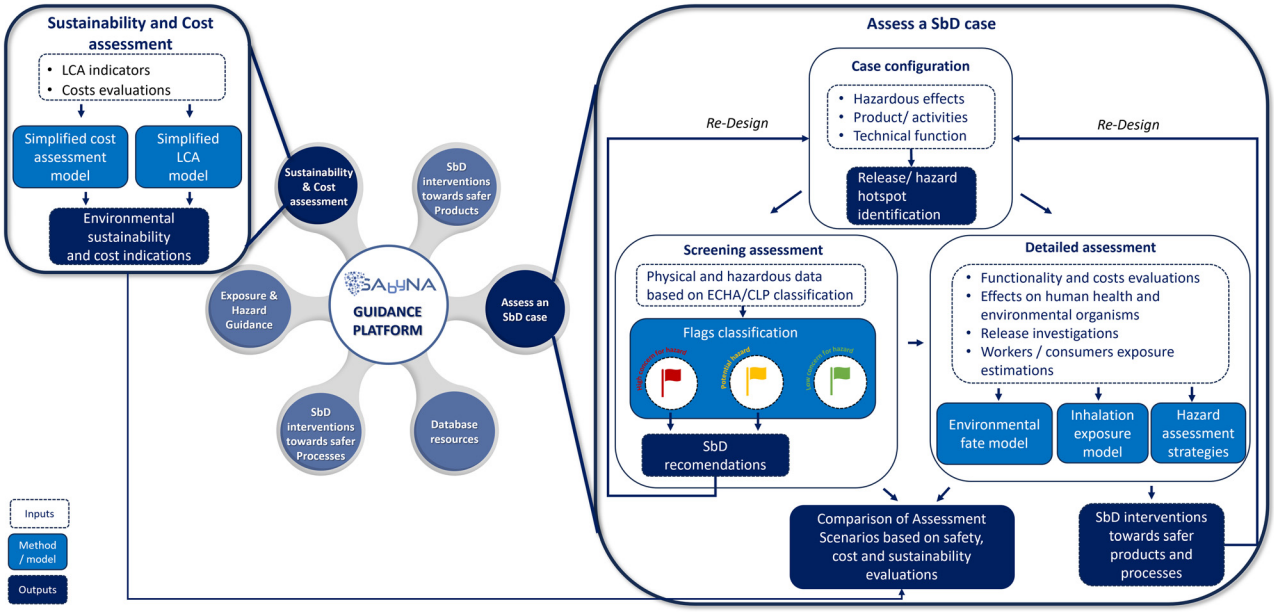

Fig. 2 General structure and flows of data/information of the two assessment modules of the SAbyNA platform.

Considering that the SSbD Framework allows an iterative approach while carrying out the evaluation,[7] this module provides resources to start the simplified assessment at the early stages of development, as suggested in the Methodological Guidance for the SSbD Framework.[7] This strategy facilitates overcoming existing limitations in the application of LCA methodology to innovative materials and processes with a low maturity level, and to NFs in particular. Some of the main limitations of the application of LCA to NFs include the scarcity of life cycle inventory (LCI) data to evaluate the production of NFs on an industrial scale and the lack of an official version of characterization factors of the emissions of NFs to toxicity and ecotoxicity impact categories.[24–26] The results of the simplified and iterative approach proposed enable the identification of hotspots (*e.g.*, points of high release, materials/processes with the highest impacts) and priorities for further data gathering to carry out an exhaustive LCA.

Focused on the two sectors investigated in SAbyNA (paints and additive manufacturing), the developed module provides an initial overview of potential impacts based on several simplifications and considers additional aspects relevant to the analysis, such as key performance parameters.

The simplifications in the proposed LCA approach compared to the full LCA include some limitations regarding the number of impact categories assessed, as well as the data gathered for the life cycle inventory.[27–32]

Concerning the limitations in the number of impact categories assessed, this is a widespread strategy in simplified LCA,[27,30,31] and in this case, it leads to the calculation of 4 main impact indicators: global warming potential, human toxicity, freshwater ecotoxicity and cumulative energy demand.

Two important simplifications were also included in the life cycle inventory:[27] the simplifications in terms of processes and inputs/outputs considered, and the substitution of primary data by secondary data.

Regarding the simplifications in terms of processes and inputs/outputs, the SAbyNA sustainability and cost assessment module have identified, on the one hand, the most significant process over the life cycle, and on the other hand, the key inputs and outputs to be quantified, based on the main environmental hotspots that could lead to impacts in the paints and additive manufacturing sectors (*i.e.*, elements of the products/processes of these sectors that can affect the environment). These simplifications are aligned with the goal of the model already mentioned.[27–29]

In terms of the substitution of primary data with secondary data, both inputs and outputs are covered,[27] and different strategies have been adopted in this context. To evaluate the environmental implications of the materials (polymers, metals, solvents, NFs, *etc.*) and energy carriers (electricity, natural gas, *etc.*) consumed during the life cycle, this module provides background data on their environmental profiles. The environmental profiles in this module comprise the pre-calculated life cycle impact assessment results for the impact categories assessed from a cradle-to-gate perspective (*e.g.*, contribution to the global warming potential of 1 kg of each material). The environmental profiles are based on public databases and literature sources, such as in the case of nanomaterials[33–38] and energy carriers.[39,40] Considering that early in the design phase, low information may be available to model downstream processes, such as industrial/professional activities, involving NFs (*e.g.*, additive manufacturing processes), the module includes basic information to cover data gaps from literature-based data. For example, in the case

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of the sustainability and cost assessment module developed for the additive manufacturing sector, a set of process steps or subprocesses has been pre-defined (classified as pre-processing, manufacturing and post-processing steps) to model the production phase of the NEP. These process steps are linked to literature-based data regarding the energy consumption and material loss rate in each one of them.[35,41–45] Section ESI† S3 illustrates some of the additive manufacturing processes considered and their energy consumption according to the literature.

Transfer coefficients (TCs) have also been proposed to model the material outcomes over the life cycle stages. TCs describe the partitioning of a material or substance in a process.[46] In this context, the module includes preliminary TCs to estimate the potential flow of NFs (to waste, air and water) during use and end-of-life phases based on existing literature findings.[47–49] Several estimations are necessary to cover the existing data gaps. However, because of the flexibility and modular structure of the platform, future developments in this field will enable the updating of the proposed TCs with more accurate information.

Based on the background information included in the model, building the simplified life cycle inventory in the sustainability and cost assessment module requires a limited set of data for a basic evaluation. For example, to evaluate the sustainability of NEP manufactured *via* additive manufacturing, the user is requested to provide at least the following information:

- Data regarding the material entering the main additive manufacturing process (*e.g.*, FDM), such as weight and material content.

- Main layout of the processes involved in the manufacturing of the NEP, starting from the main manufacturing technology (*e.g.*, FDM) but potentially adding pre-processing and post-processing operations (*e.g.*, mixing and filament extrusion), which are selected among the options provided by the module.

- Expected use phase scenario characteristics (*e.g.*, indoor/outdoor use and durability).

- End of life operations foreseen (rate of product expected to be recycled, landfilled or incinerated).

To illustrate this approach, Fig. S2 ESI† S3 shows a simplified representation of the key data and parameters used to build the LCI in the additive manufacturing sustainability and cost assessment module based on the production phase. The module can calculate a basic inventory starting from the minimum inputs mentioned above (materials entering the manufacturing phase and definition of the process steps involved). Simultaneously, the energy consumption in each step is also based on the background data provided within the module.

Although it is possible to conduct a preliminary assessment based on the default data provided, the SAbyNA sustainability and cost assessment module enables the iterative approach applicable in the context of the SSbD framework,[7] enabling the user to customize all default values and parameters, either to improve data quality or to check different scenarios. Moreover, further details on specific environmental aspects can be added, such as the consumption of auxiliary materials in each process step, or the efficiency of air emission control systems in place. Additionally, further processes can easily be included in the background data.

The LCI built into the model is the input for the life cycle impact assessment. Additionally, in this step, the model is constructed to provide support for the assessment, integrating characterization factors to evaluate the contribution of the released NFs to human toxicity and freshwater ecotoxicity impact categories, providing default values for specific materials based on the literature.[50–54] The number of characterization factors for NFs is also expected to increase according to developments in the field.

The SAbyNA sustainability and cost assessment model finally calculates simplified LCA indicators for each scenario modelled as follows:

- Global warming potential (kg CO_2 equivalents),
- Cumulative energy demand (MJ),
- Human toxicity (disability adjusted years),
- Freshwater ecotoxicity (potentially disappeared fraction).

To support the interpretation of the results, considering the uncertainty linked to the above-mentioned simplifications and limitations, all results are presented with minimum and maximum values. Additionally, five scenarios can be modelled in parallel, making it possible to check the relevance of different variables in the results.

Regarding the cost analysis, in this case, a simplified approach is proposed based on data derived from the user, which can be further detailed in a more exhaustive assessment. The life cycle stages and processes defined in the simplified LCA, together with the data associated with them (production processes and subprocesses, material and energy flows, durability, performance of the products, *etc.*), constitute the basis for the construction of the cost model. Indeed, the approach proposed in this module is mainly focused on costs associated to the requiring data to quantify different cost elements such as raw material costs, duration of the synthesis process, yearly productivity of the NF/NEP, electricity consumptions and costs, costs of equipment, including costs associated to the potential SbD measures implemented. However, performance-related data influencing the costs associated with the use phase of the product can also be considered. The simplified results obtained in this evaluation are relative values, reflecting the relative cost difference of each SbD scenario compared to a base case scenario.

Assess an SbD case

Case configuration. In this module, the first section invites the user to configure the case by providing information on the NF/NEP and related use scenarios in alignment with ECHA,[10] such as characteristics of the NFs,

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available toxicity data, use and activity/process steps performed by the workers to produce the candidate NF/NEP. Therefore, the platform suggests potential releases to be considered for each stage of the NF/NEP life cycle as well as each potential substance/product generated.

Screening assessment. The screening section is the starting point of the SbD case assessment and can support users with both a theoretical and an existing baseline NF. The screening section first assists the user in exploring nanoform types known to fulfil the desired technical function(s), if needed. Proceeding with a nanomaterial type in mind, the module provides a list of associated (bulk) substances that are known to be present in nanoforms on the EU market (European Union Observatory for Nanomaterials (EUON)). These substances identified by their EC numbers are presented to the user to select one or more NF. In case a better representative EC-number exists, which is not yet listed in the platform, the user can provide it directly. In addition, basic information on the (intended) NF, such as composition, crystallinity, size, shape and specific surface area, must be provided or estimated, without considering the matrix (*e.g.*, if the NF would be added in a dispersion). Finally, human exposure and/or environmental emission routes along an NF's life cycle should be indicated.

The provided information is then used by the screening assessment module to inform about known hazard indicators related to 1) physical hazards, 2) general human health hazards, and 3) general environmental hazards. To generate this screening outcome, the platform uses several internal resources, such as a set of warning rules based on hazards related to physicochemical properties, and a database with existing CLP classification[55,56] related to the bulk material or NF. For each identified concern, a red, orange or green flag with a suggestion on how to proceed is raised by the platform based on the information source and hazard type. In the case of obvious high hazard concerns (red flags) with the envisioned nanoform, an SbD intervention is directly suggested. In other cases (orange flags), a more thorough assessment is suggested (detailed assessment). Only general concerns or those related to the indicated likely exposure routes are used for the final screening outcome. In addition, the screening phase cannot be sensitive enough to differentiate between modified NF alternatives when different alternatives fall into the same hazard category. In this case, a detailed assessment is suggested to investigate more deeply the differences between SbD alternatives. More information on the screening hazard assessment can be found in ESI† S4.

Detailed assessment. Once the screening assessment is completed, a more detailed understanding can be reached by the user on information related to the exposure, hazard and functionality assessment of the (re)designed NF/NEP.

Once routes of exposure and/or environmental compartments potentially affected by an NF release are detected in the screening assessment section, exposure estimations can be made using a fate model, which can be used for occupational exposure quantifications and environmental exposure estimations. This kinetic fate model is a reimplementation of the one already developed in the GUIDEnano tool to support the assessment of the fate of released NFs. For each assessment scenario, measured data or derived estimations of the exposure receptor can be added. Then, based on kinetic fate calculations and considering the environmental compartment in which the NF will end up, as well as the risk management measures used, exposure estimations are obtained. This fate model estimates the exposure concentration in particle number and mass as well as the particle size distribution, starting with the identification of the relevant physical and chemical processes that may occur in and between all compartments found within the case. Simultaneously, it also introduces any new species in the related zones as a consequence of the identified transport, reaction and transformation processes. The species originated from releases and all became part of a mixture of exposure-relevant agents in the different zones. For each of these species, the fate model is capable of source apportionment, that is, to be able to trace species back to their release(s). This is invaluable information for SbD interventions, enabling them to target specific release hotspots. Each time a user modifies the case scenario, the fate is reassessed automatically. The fate model can also be used to simulate the exposure concentrations over time of the identified species in all zones. These concentration estimates can be used to follow the predicted kinetic behaviour and derive time-weighted average or compartment-specific predicted environmental concentrations (PECs). The fate model is extendable such that new processes can be integrated. The current version contains several physical transport processes, such as advection and settlement, and few chemical reactions.

In the detailed human hazard assessment, the user is guided towards hazard strategies tailored for inhalation, dermal and oral routes of exposure and fully based on new-approach methodologies (NAMs) requiring non-animal testing. Hazard assessment strategies can be effectively used to compare the potential toxicity of different NF design alternatives or to confirm the reduction in the toxicity profile of an NF after the suggested SbD intervention. In the case of predicted inhalation exposure, information on the NF/NEP dissolution rate in lung physiological fluids, cytotoxicity, genotoxicity, reactive oxygen species generation, and inflammation is required. For dermal exposure, additional endpoints such as dissolution in sweat-simulated fluids, skin irritation and sensitisation, and dermal absorption are also considered. A preliminary version of an oral hazard strategy is currently provided, which will be fully developed in future versions of the platform after being tested and applied to a real case study. To fill the different inputs required in the hazard strategy, the user can gather existing data in the literature or databases or can generate new data by following the guidance documents in which *in vitro* assays are suggested. The testing strategies consider *in vitro* assays of different levels of complexity, following or not standardised

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protocols, and retrieving outcomes with weaker or stronger scientific evidence; new or alternative, more reliable methods can be added in the future, based on the latest state of the art, owing to the flexibility of the platform. For each toxicity endpoint, the user should introduce data into the platform, obtaining an outcome in the form of a coloured scale of levels of concern established in the guidance. Green or blue colour indicates the lowest level of concern, with the colour allocated according to the level of confidence in the test method applied, with less complex and unstandardised assays denoted in blue. An orange colour indicates a moderate concern with some indications of toxicity. Finally, the red colour indicates a high toxicity response and therefore a high level of concern; here, the platform will suggest considering an SbD intervention to reduce the potential hazard endpoint.

The detailed environmental hazard assessment aims to derive harmonised effect threshold concentrations for the candidate NF(s) and is based on existing methods.[57] Threshold concentrations can be derived either from existing data or from the targeted generation of relevant new data, where the relevant environmental compartments are already identified in the case configuration section. This is an example of how different sections of the platform can provide feedback to one another and improve the efficiency and relevance of an assessment of an SbD case. Full details of the methodology for the detailed environmental hazard assessment are available in the environmental hazard strategy section of the platform. The effect threshold concentrations provide a hazard indicator to support decisions around SbD options, where comparison of the derived effect thresholds against thresholds for aquatic and terrestrial organisms allows the NF to be assigned to hazard indicators of very toxic, toxic, hazardous or not categorised.[58,59] Alternatively, the effect thresholds can be delivered to a comparative assessment to evaluate different SbD options against their environmental safety.

To extract an indication of hazard from the available ecotoxicity data, the chronic NOEC of a single test or the median hazardous concentration (the HC50) from a species sensitivity distribution (SSD) is compared with the thresholds in Table 1.

If the chronic NOEC is greater than the upper limit of the "harmful" thresholds in either soil or freshwater, then the NF is considered "not categorised". These toxicity thresholds were the most suitable ones identified from the existing literature to be relevant for NFs. For consistency, these thresholds are converted from their original metrics using the same assessment factors into chronic NOECs.

Additionally, mesocosm experiments can be designed to specifically cover the aging of NEPs while characterizing their associated exposure and hazards. The scenario of exposure and the lifetime of the NEPs appear to be the predominant factors in the design of the experiment.[60]

In this detailed assessment, additional information can also be added related to the physico-chemical properties of the NF based on OECD harmonised template 1 to 23–5 for chemicals and from 101 to 113 specific for nanomaterials.[61] Moreover, the functionality of the redesigned NF/NEP can be deeply investigated by adding information related to the technical function evaluation based on ECHA categories.[62] Information related to the costs along the life cycle of the NF/NEP can be manually added by the user by providing information on the labour costs, energy, risk management measures and costs of disposal of the final NEP to visualise how the resources are used for each life cycle stage of the NEP.

Based on the inputs provided in the detailed assessment and in cases where hazard/exposure concerns are detected, *ad hoc* SbD interventions are suggested by the platform to reduce hazards and/or release the assessed NF.

Support decision making and (re)design iterations. The last section of the SAbyNA platform supports the user in decision-making processes. Once functionality, safety, sustainability and cost evaluations are added to the platform, the user can visualise the considered assessment scenarios and compare different SSbD alternatives. A comparison can be made between one or more assessment pillars depending on whether the focus of the assessment should be made. In this way, the comparison of scenarios before and after the application of one or more SbD interventions can be easily visualised by the user and recognised if the intervention reduces hazard and/or exposure or has improved sustainability, without compromising functionality. The simplified visualization of all the results obtained for the assessed NF/NEP helps the user in decision-making processes (*e.g.*, which safety and sustainability aspects can be further improved).

If the SbD intervention is not observed to improve the performance of the NF/NEP (*e.g.*, if safety is compromised or functionality of the NF/NEP is affected), a feedback loop can be made to consider different SbD interventions, returning to the case configuration to change physico-chemical characteristics of the NF/NEP and/or processes.

Application of the SAbyNA platform in a real case study

The SAbyNA platform was tested with an industrial case study to observe how the redesign of a PC loaded with SWCNTs can be assessed by the platform by implementing SbD strategies as a consequence of the screening assessment results.

Case configuration. PC filaments loaded with SWCNT were produced for their application in fused deposition modelling (FDM) 3D printing to obtain NEPs (or demonstrators) as a final product with antistatic properties provided by the addition of SWCNT, which increases the conductivity of the PC polymer. SWCNT was provided as a masterbatch by OCSiAl-Europe Sarl (Luxembourg), composed of a polyol ester matrix of 75% and a SWCNT of 25% (outer diameter: 1.6 nm, fibre length: >5 μm, and approximate aspect ratio: 5000), indicated as PC-SWCNT hereafter.

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Table 1 Final selection of hazard indicators based on thresholds for aquatic and soil environments. Chronic NOECs are compared with these thresholds to provide a hazard indication. The original contaminants for which these potency thresholds were established are PBT/vPvB substances or manufactured nanomaterials (MNM, NanoRiskCat)

EC	VT	T	H	Contam.	Source
Soil	≤ 1 mg kg^{-1}	≤ 10 mg kg^{-1}	≤ 100 mg kg^{-1}	PBT/vPvB	58
Freshwater	<0.1 mg L^{-1}	>0.1 to ≤ 1 mg L^{-1}	>1 to ≤ 10 mg L^{-1}	MNM	59

EC: environmental compartment, VT: very toxic, T: toxic, H: harmful, Contam.: contaminant for which thresholds are originally established.

Masterbatch production was also considered to investigate potential hazardous effects/releases during the initial stage of the product development.

Screening assessment. Intrinsic and extrinsic properties required in the screening assessment were reported for this NEP in ESI† S5 based on the information provided by the NEP manufacturers.

The classification and labelling and the output of the screening assessment for this NF obtained by the platform are presented in Fig. 3. According to the CLP information, this NF is considered hazardous as it causes serious eye irritation, fulfilling the lowest concern category according to the JRC SSbD document (H3). Consequently, actions to reduce the irritating effects (presented as an orange flag) or to ensure that the NF can be safely handled along the life cycle are recommended (presented with two red flags), while no environmental concerns are reported for any of the environmental compartments (green flag). The two red flags obtained referred to the possibility of hazardous effects as a consequence of the inhalation exposure of SWCNTs, classified for their PC property as high aspect ratio nanomaterial (HARN), which raises a concern for inhalation hazard (asbestos-like materials raise a concern for mesothelioma[63] and high dustiness), while dermal and oral exposure were considered unlikely. SbD recommendations were suggested by the platform to reduce this potential hazard by modifying the morphology of the SWCNTs (*e.g.*, by reducing fiber length or rigidity) or by changing process parameters to reduce the emissions of fibers and consequent inhalation exposure of these NFs (*e.g.*, avoiding high energy process/activity).

Detailed assessment. To provide more details on the potential hazard/exposure along the life cycle of the NF/NEP, use scenarios, upstream/downstream products and intermediate compounds were identified along the PC-SWCNT product life cycle and added in the platform evaluation through a continuous engagement with the manufacturers. More specifically, volatiles organic compounds (VOCs) as potential released substances, upstream products (*e.g.*, SWCNT, polycarbonate and

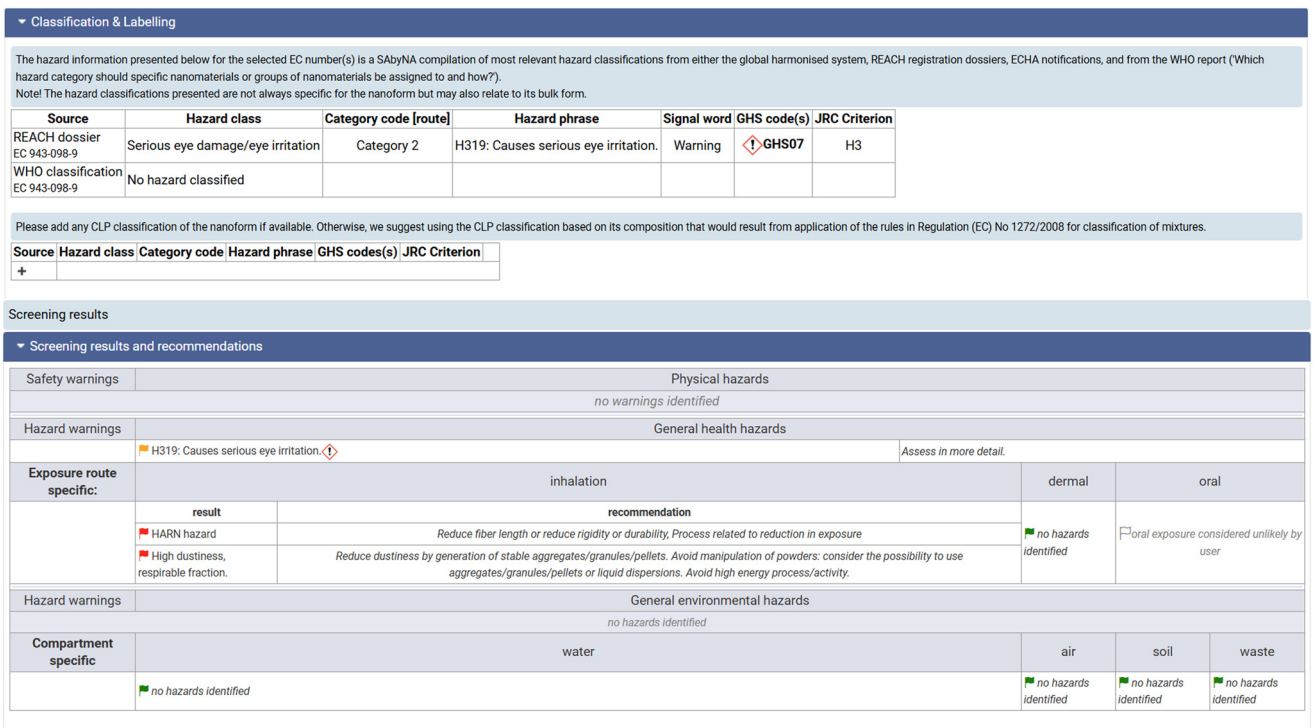

Fig. 3 Classification and labelling (top) and screening results and recommendations (bottom) of the SWCNT obtained by the platform.

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confidential ingredients), intermediate products (*i.e.*, the TUBALL matrix) and downstream products obtained by changing the temperature and infill density were identified for the PC-SWCNT product.

By adding this information, the platform can present the material/substance form or use-stage as single tiles for each life cycle stage of the PC-SWCNT ("product value chain" section, left part of Fig. 4) and define if it is a mixture, NEP or NF. The small sign on the bottom part of each tile indicates the possibility of released material and the potential of hazard/exposure concerns (*i.e.*, white/orange triangle if the substance is used as input, output and/or released and red disc if the activity has potential exposure hotspots). Contributing activities are shown by the platform in the centre part of the image, where use scenarios are reported for the different stages of the life cycle using the same triangle indications. Considering the compartments and receptors section (right part of Fig. 4), a visual representation shows where the substances are released into or transported towards (*e.g.*, house symbol for indoor application and sun/cloud representation for outdoor air use), which receptor can be exposed to (*i.e.*, worker, general population, and environmental organisms) and if a risk management measure is used (*e.g.*, air ventilation system). From this overview, it is possible to map and identify all the potential hotspots of release along the life cycle of the NEP (*i.e.*, all the activities marked by a red disc).

Among the SbD recommendations provided by the platform for this NF, in this study, avoiding high energy processes/activity was considered an SbD intervention to reduce the potential inhalation exposure of workers during the manufacturing of this NEP. Therefore, the reduction in temperature during the 3D printing process was considered an SbD intervention to decrease the particle concentration emitted at the manufacturing site, thus reducing the inhalation exposure of potential workers. More specifically, a reduction in manufacturing process (3D printing) temperature from 290 °C to 270 °C and 250 °C was adopted as an SbD intervention, generating the corresponding PC-SWCNT.290, PC-SWCNT.270, and PC-SWCNT.250 NEPs. In addition, as the infill density (3D printing process parameter) can affect the release of particles during the 3D printing process, an infill density of 50% was considered with 270 °C as the SbD strategy, obtaining the PC-SWCNT.270-50% NEP. Once the SbD strategy is implemented and safety is investigated, technical function, sustainability and cost performance are evaluated to check if the SbD intervention is affecting these aspects.

In the current work, four contributing activities were investigated to compare functionality, cost and sustainability aspects and inhalation exposure before and after the application of the SbD intervention (Table 2), while for hazard assessment, the comparison was made between the PC-SWCNT, the PC and the SWCNTs. Data used in each section and the output obtained from the platform are presented through a comparison of the NEP before and after the implementation of the SbD intervention in the following paragraphs.

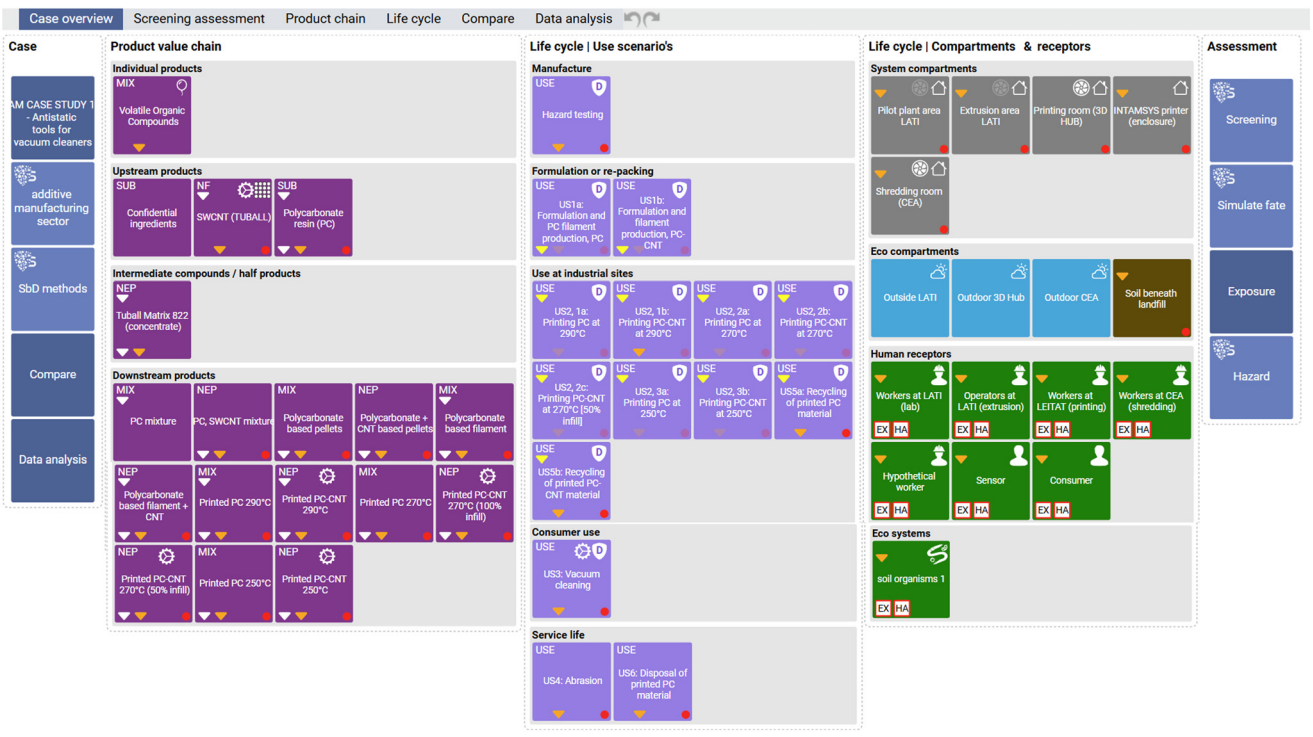

Fig. 4 Overview of the substances/materials used, compartments considered and exposure target for the different contributing activities of the PC-SWCNT case study.

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Functionality evaluation. All the NEPs produced with different nozzle temperatures and infill densities during the 3D printing process were first tested for their functionality, thus ensuring that the antistatic property is maintained after the application of the SbD intervention.

Antistatic properties were evaluated by testing the conductivity of the NEPs using an insulation resistance tester (applied voltage = 100 V). More details on the method and technique used are included in ESI† S6. The results indicate that the application of the SbD strategies involves a reduction in the nozzle temperature; a reduction in infill density causes only minor deteriorations in the conductivity of 3D-printed objects (from 10^8 Ohm of the initial PC-SWCNT to 10^9 Ohm after SbD interventions), and PC-SWCNT retains its antistatic properties after the implementation of the SbD interventions. Based on the manufacturer's judgement, results obtained are then added to the platform considering 100% functionality for the PC-SWCNT and 90% for all the other NEPs (*i.e.*, PC-SWCNT.270, PC-SWCNT.250, and PC-SWCNT.270–50%) and reported in ESI† S7.

Sustainability evaluation. The application of the SAbyNA cost and sustainability assessment module is tested in the simplified analysis of the potential environmental and economic implications in the life cycle of filaments incorporating SWCNT for additive manufacturing (fused deposition modeling (FDM)) as mentioned above. The life cycle of the PC-SWCNT nanocomposite is modelled, which reflects processes together with material and energy flows, leading to the identification of potential data gaps or/and environmental priorities. The reduction in process temperature, which is expected to lead to a significant reduction in energy consumption, is also a relevant aspect of this assessment that requires additional analysis to validate it empirically. To assess the dimension of the potential influence of this process in energy reduction, different scenarios were evaluated: the base scenario (based on data from the literature) for the manufacturing phase, a second scenario with a 5% reduction in energy consumption in the manufacturing phase, and a third scenario with a 10% reduction in energy consumption in the manufacturing phase. These reduction rates have been proposed as reference points to evaluate the relevance of this aspect and are associated with temperature reduction in the manufacturing process. In terms of costs, the data availability for industrial-scale additive manufacturing is limited; therefore, an approximated scenario has been modelled considering the costs for material and key processes (*e.g.*, labour). The information was collected through industrial partners in the SAbyNA consortium and a literature review.[64,65]

The results of the simplified sustainability analysis show that an energy reduction of 5% or higher in the FDM energy consumption can lead to an environmental improvement according to the four impact categories assessed (Fig. S6a†). This result is consistent with the results in the literature, where energy consumption in FDM is the most significant contributor to CO_2 emissions and cumulative energy demand,[64] indicating that this is a major hotspot to be further evaluated in SbD implementation owing to the large uncertainty in data at this stage. The use of the module to assess further scenarios demonstrates that when the energy reduction is lower than 3%, three of four impact category indicators present very reduced improvement (<1%). The contribution of the potential outdoor release of NFs to toxicity and ecotoxicity impact categories is not significant for this case study. Regarding the indoor emission, the SWCNTs were not released in the production site owing to the physicochemical state (dispersion) and the emission

Table 2 Aspects assessed (impact category/functionality indicator/route of exposure) and materials tested for each contributing activity (CA) considered. The initial material is highlighted in bold

Assessm. pillar	Aspects assessed	Type of data	CA	Tested material/product
Function	Antistatic property	Experiment. data	CA3: use stage	**PC-SWCNT.290** PC-SWCNT.250 PC-SWCNT.270 PC-SWCNT.270-50
Cost and Sustainab.	Energy consum.	Literature data and modelling	CA1: formulat. and product. of NEP	**PC-SWCNT.290** PC-SWCNT.250 PC-SWCNT.270
Release/exposure	Inhalation	Experiment. data	CA2: 3D printing process – filament extrusion	**PC-SWCNT.290** PC-SWCNT.250 PC-SWCNT.270-50 PC-250 PC-270 PC-290
Hazard	Inhalation	Hazard strategy: experiment. and literat. data	CA4: shredding materials for recycling	**PC-SWCNT.290** PC SWCNT

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prevention measures adopted. In addition, the release of the SWCNTs during the use phase was considered very limited as the SWCNTs were embedded in the PC matrix. The simplified LCA inputs were added to the platform to compare the different SbD alternatives, as reported in ESI† S8.

Regarding the simplified cost assessment, the main cost contributors are the material and labour costs of the assessed NEP. Energy demand has proven to be a relatively low contributor to the overall costs, but there is a slight reduction in the manufacturing phase owing to lower energy consumption. As shown in ESI† S8, the differences in the cost of production of the PC-SWCNT produced at different nozzle temperatures are minimal, which does not allow discrimination between the different SbD alternatives.

Release assessment. An air monitoring campaign was performed to investigate particle release during 3D-printing of the PC-SWCNT filament when different nozzle temperatures were applied. Online measurements using direct reading instruments and offline analysis of collected samples ensured a complete characterization of the particles released using particle counters, transmission electron microscopy (TEM) and inductively coupled plasma-mass spectrometry (ICP-MS) analysis. Additional details related to the emission characterization can be found in the study by McLean *et al.* (2024)[66] and in ESI† S9, where indications of potential usability cards to be used for this specific case study can be found.

The highest emissions were monitored with nozzle temperatures of 290 °C, reaching a concentration above 10^6 particles per cm^3 (PC-CNTs: 3.84×10^6 particles per cm^3; PC: 1.90×10^6 particles per cm^3). A twenty-degree reduction in the nozzle temperature to 270 °C led to a reduction in almost one order of magnitude of the emitted particle number concentrations (PC-CNTs: 3.80×10^5 particles per cm^3, PC: 1.74×10^5 particles per cm^3). A further decrease in nozzle temperature to 250 °C additionally reduced the emitted concentration by a factor of two during the 3D-printing of the PC-CNT filament (1.76×10^5 particles per cm^3) and above one order of magnitude for the PC filament (6.22×10^3 particles per cm^3).

Considering the change in the second process parameter, the 50% reduction in the infill density led to a reduction by a factor of two in particles emitted (LI_PC-CNTs_270: 1.86×10^5 particles per cm^3) when compared to the 100% infill density (PC-CNTs_270: 3.80×10^5 particles per cm^3). Particle concentrations were added as inputs in the platform to visualise the differences between the SbD alternatives and the baseline material together with the characteristics of the monitoring site (Fig. 5). Based on the results obtained by ICP-MS and TEM analysis of the collected filters, emissions of nanometric particles were not dependent on the content of SWCNT, but the emitted aerosols were mainly process-generated. Further information is available in ESI† S9.

Toxicological assessment. The detailed hazard assessment focused on inhalation exposure to IATA to compare the potential toxicity of the different alternatives. Information on

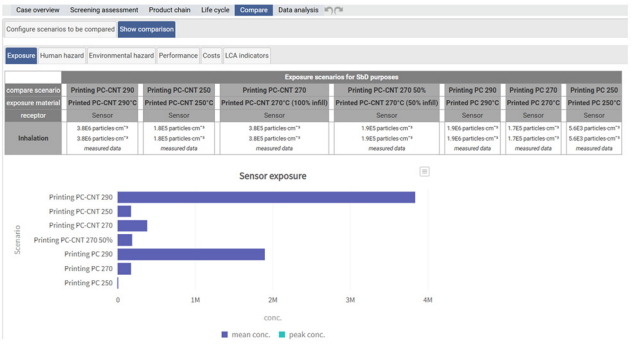

Fig. 5 Comparison of release results obtained by the air monitoring campaign performed before (*i.e.*, PC-SWCNT.290) and after SbD implementations (PC-SWCNT.250, PC-SWCNT.270, and PC-SWCNT.270-50%) as well as during the production of the PC without SWCNTs (*i.e.*, PC-290, PC-270, and PC-250).

each toxicity endpoint included in the inhalation testing strategy was obtained either by searching the literature or by performing *in vitro* assays using several human lung cell models exposed to a range of concentrations of the cryomilled materials (*i.e.*, PC and PC-SWCNT). SWCNT TUBALL is used as a reference material to perform the comparison.

Toxicity data on SWCNTs found in the literature were sometimes contradictory, mostly related to the difference in purity of the studied materials or attachment of functional groups, and specific data for SWCNT TUBALL were not always possible to obtain. Some studies using rat lung epithelial cells and HEK293 cells showed cytotoxicity and cell proliferation inhibition by SWCNTs, while others did not show any, even at very high exposures.[67–69] However, during our *in vitro* testing, we did not find evidence of cytotoxicity after exposure to several pulmonary cell lines when SWCNTs were tested in parallel with the other cryomilled materials. A published genotoxicity assessment using a battery of assays comprising a bacterial reverse mutation test, an *in vitro* mammalian chromosomal aberration test and a mammalian erythrocyte micronucleus test showed no genotoxic risk of SWCNTs.[70] Regarding ROS production, it has been reported that exposure of SWCNTs to rat lung epithelial cells induces oxidative stress.[69] Results from inflammation studies were also often contradictory. For example, SWCNTs showed no effect in inducing an innate immune response at subtoxic doses in mouse macrophage cells.[71] Furthermore, SWCNTs did not induce neutrophil inflammation in the lungs in an *in vivo* study.[72] Moreover, in a different study, SWCNTs were found to elicit acute inflammation and the onset of progressive fibrosis and granulomas in the lungs of C57BL/6 mice.[73] Regarding biodurability, SWCNTs were found in mice lung tissue after 1 year of *in vivo* exposure and were therefore classified as persistent.[74] The classification as persistent in lung fluids is also in line with the classification made for the HARN IATA of MWCNT.[63]

In the case of PC and PC-SWCNT materials, information regarding the dissolution in lung fluids was also extracted

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from the literature, where the deposition of PC filaments emitted during the heating process for 3D printing was detected in the alveolar region of the one-day and 30 day exposed rats.[75] Therefore, materials are classified as persistent, and no colour code is used in that case, as the dissolution endpoint does not imply more or less toxicity of the material; it adds only information that can help interpret the results in the other endpoints and to continue the hazard pathway of the NF. The cytotoxicity assessment was performed in different pulmonary cell lines exposed to the materials, and cell viability was analysed using MTT, WST-1 and LDH assays. The results are fully described in Polanco-Garriz *et al.* (in preparation).[77] Briefly, all the results obtained indicate low cytotoxic potential for all the CS materials, classifying them for the blue "low concern" code. Genotoxicity was tested using an *in vitro* micronucleus assay in TK6 cells (OECD TG487). The results obtained indicate a low genotoxic potential for PC and PC-SWCNT, receiving a low concern code. The acellular ferric reduction ability of serum (FRAS) assay indicated low potential for oxidative damage classified as a blue, low concern category. The pro-inflammatory potential of the CS materials, assessed using Legendplex, indicated low inflammatory responses, and a blue-coloured low concern category was obtained. All the details for each endpoint tested and the corresponding classification obtained by the platform are reported in ESI† S10, while the final comparison is illustrated in Fig. 6.

The results obtained from the comparison showed no differences in terms of toxicity between the ground PC and PC-SWCNT for each endpoint assessed. Compared with the literature data on SWCNTs, the combination with PC-SWCNTs appeared to improve their toxicity profile, lowering concerns regarding ROS and inflammatory potential. However, all the materials should optimally be tested in parallel for comparison to be more reliable.

The outcome of the inhalation IATA in the hazard assessment is displayed by the platform, which is the same for PC and PC-SWCNT materials: "Poorly soluble materials with low reactivity and low inflammation potential, no concern for acute toxicity. Potential concern for long-term toxicity in case of long-term high dose exposure. No concern in the case of low exposure".

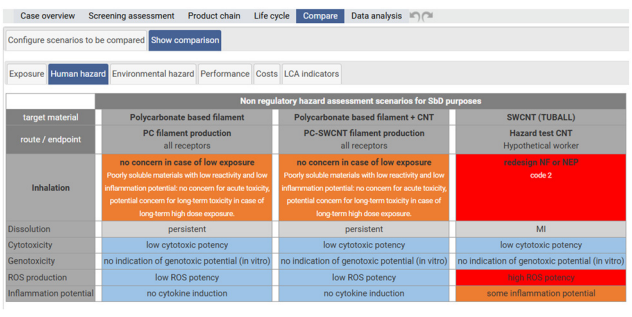

Fig. 6 Comparison showed in the platform considering the added toxicological results for the SWCNT, PC-SWCNT and the PC without SWCNT.

This indicates that no concerns were detected by the platform for all the activities in which a low level of inhalation exposure of workers was predicted for PC and PC-SWCNT. When the hazard of poorly soluble low toxicity particles are assessed, an orange flag is raised to indicate that long-term (chronic) high dose exposure (in real-life scenarios) may lead to accumulation, which might then impact the lungs.[76] More details can be found in ESI† S8. Considering the SWCNT without a polymeric matrix, the redesign of this NF was suggested by the platform to reduce hazard concerns because of its effects on ROS and inflammatory potential (indicated with a red and orange flag, respectively).

To conclude, the reduction in nozzle temperature and infill density is demonstrated to be an efficient SbD strategy for reducing particle emissions during the manufacturing of the NEP, reducing energy consumption, while maintaining the same functionality. Hazard results showed that once SWCNTs were embedded in PC polymers, no hazard concerns were detected in the case of low inhalation exposure.

Discussion and conclusion

There is a broad consensus on the need for SSbD and its benefits, while certain areas of application and development remain uncertain. The SAbyNA platform is a practical, usable, and scientifically grounded tool that addresses industry needs and concerns, helping take one large step further towards safety and sustainability for NMs and NEPs. The SAbyNA platform integrates, in a single tool, the assessment of human and environmental safety, costs and sustainability aspects and the suggestion of appropriate strategies to reduce or mitigate risks from NFs and NEPs along their life cycles.

The SAbyNA platform is not intended to provide standardized guidelines for manufacturing NEPs. Instead, it serves as a decision-support tool for innovators, engineers and managers, risk assessors and researchers, enabling them to make informed choices that prioritize safer and more sustainable NEPs and their components. To achieve this, the platform incorporates knowledge generated in previous projects through the inclusion of data, methodologies, IATAs, models and tools that have been either directly integrated or adapted for SSbD to perform basic early-on-evaluations through a collaboration of an interdisciplinary team. The division between informative and assessment modules permits not only to perform safety and sustainability assessments of NFs and NEPs but also to use the platform to check, in an easy-to-use way, sources of information that can help with the assessments (*e.g.*, how to use the simplified LCA guideline, in which the release/exposure test is appropriate for the assessed NF/process, *in vitro* tests used and corresponding thresholds in the hazard IATAs).

However, integrating safety and sustainability considerations in the early stages of the design of NFs and NEPs involves a certain degree of uncertainty based on data quality and completeness. In this regard, one of the goals of

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the SAbyNA platform was to reduce this uncertainty as much as possible and provide the user with information and a rational decision to guide the design of NEPs and processes as safely and sustainably as possible. This was achieved through the visual detection of data gaps in the platform along with the safety and sustainability assessments, informing the user about the fields where providing additional information would increase the quality of the prediction.

This study details the application of the platform in the PC-SWCNT case study to demonstrate the usability of the tool in real industrial environments. It has been shown that once information on the physico-chemical characteristics of the investigated NF was inserted, the green/orange/red flag system quickly identified hazard concerns of the SWCNT to the user. Moreover, the SbD strategies proposed in the screening assessment of the platform gave indications on how the PC-SWCNT can be modified/used to reduce hazard and exposure concerns. Once the SbD intervention was applied to this NEP (*i.e.*, the reduction in nozzle temperature during manufacturing and the infill density of the NEP), its performance was verified in terms of functionality, safety and sustainability evaluations. At the end of the assessments, the platform allows a comparison of the different materials, aiming to verify how the selected SbD strategies (reduction in nozzle temperature and infill density) reduced the release of airborne particles during the manufacturing of the NEP and positively affected environmental sustainability through a reduction in cumulative energy demand and global warming potential categories. In addition, the detailed hazard assessment based on the inhalation exposure IATA showed that once SWCNTs were combined with PC, their toxicity profile improved, with lowered concerns regarding ROS and inflammatory potential. Moreover, in the hazard assessment, no concerns were detected by the platform for all the activities where a low level of inhalation exposure of workers was detected for both PC and PC-SWCNT. During the entire assessment, the user has access to the informative modules of the platform, allowing access to specific SbD strategies, guidelines/protocols to conduct a more exhaustive workers' exposure assessment, and the *in vitro* tests proposed in the human health inhalation IATA strategy.

It is worth highlighting that a correct interpretation of the results obtained from the platform as well as the final decision making in this case require a high level of knowledge in both safety and sustainability assessments.

To conclude, the SAbyNA platform has been designed to assess the safety and sustainability of NFs and NEPs. Because of its flexibility, this digital guidance tool can be modified and tuned for other innovative materials or processes (*e.g.*, advanced (nano)materials, generated micro and nanoplastics), adding advanced hazard strategies based on new advanced methodologies (NAMs) and advanced outcome pathways (AOPs), as well as including social and more detailed economic sustainability aspects. In addition, multi criteria decision analysis (MCDA) would potentially be used to support decision making in the comparison of different alternatives by considering the weight of different criteria assessed based on the objectives to be achieved, as explained by Dias *et al.* (2024).[78] Another aspect to be potentially further developed would be to better investigate and organize sustainable-by-design strategies as already done in the past for the safety counterpart by identifying sources of information (*e.g.*, guidelines/scientific papers) that can support the implementation of sustainable aspects at the design stage of the product development (*e.g.*, recyclable-by-design alternatives to promote circularity, ecodesign principles, re-use applications of the NEP and/or the single NF).

Data availability

The data supporting this article have been included as part of the ESI.†

Author contributions

Writing (original draft): V. C. Methodology and investigation: V. C., R. V., J. H., A. S. H., S. H., M. A., H. B., M. B., A. C., A. K., I. R. L., J. C., R. K. C., E. L., E. M., F. C. S., C. D., S. C., R. S., A. S., L. B., L. T., D. L., C. M. Writing (review and editing): J. H., A. S. H., M. B., J. C., R. K. C., E. M., C. M., S. V. C. Software: R. V., L. T., Funding acquisition: S. V. C. Project administration: S. V. C.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 862419. This publication reflects only the authors' views, and the European Union is not liable for any use that may be made of the information contained herein. The authors thank all the partners who contributed to the development of the SAbyNA guidance platform.

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