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Identification of emerging safety and sustainability issues of advanced materials: Proposal for a systematic approach

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ABSTRACT

The EU Chemicals Strategy for Sustainability is a first step to achieve the Green Deal ambition for a toxic-free environment, and ensure that chemicals are produced and used in a way that maximises their contribution to society while avoiding harm to our planet and to future generations. Advanced materials are predicted to play a pivotal role in achieving this ambition and the underlying sustainability goals, and considerable efforts are invested in designing new classes of materials. Examples of such materials are metamaterials, artificially architectured materials designed to have material properties beyond those of the individual ingredient materials, or active materials at the boundary between materials and devices (e.g., new biomedical soft materials). Such innovative advanced materials raise concern about possible future safety and sustainability issues and would benefit from appropriate risk governance that promotes innovation, while pushing for safety and sustainability. To balance these aspects, a methodology is proposed for the early-stage identification of emerging safety and sustainability issues of advanced materials. As exemplified by two case studies, the methodology aims to be of use for innovators, risk assessors, and regulators. Extension of the methodology is highlighted, as well as implementation in broader initiatives like the EU's industrial policy approach.

1. Introduction

The European Green Deal (GD), the European Union's new growth strategy (EC, 2019a), has set the EU on an urgent course to become a sustainable climate neutral and circular economy by 2050. It has also set the goal of better protecting human health and the environment as part of an ambitious approach to tackle pollution from all sources and move towards a toxic-free environment, as for example outlined in the EU's chemicals strategy for sustainability (EC, 2020) that is part of the GD. The GD defines the Commission's commitment to tackling climate change and environment related challenges, setting ambitious goals like a zero-pollution approach for a toxic-free environment. Major investments in cutting-edge research and innovation and the new Framework Programme Horizon Europe (Gottardo et al., 2021) based on modern innovation principles, are put in place to achieve these transformative objectives.

The development of so-called advanced materials is thought to be critical to reaching some of the transitions and goals of the European GD. Advanced materials are central to the design of innovative technologies and products that are ranging from systems engineering to energy harvesting and energy storage, to biomedicine (EC, 2020). These advanced materials thus play an increasingly important role, e.g. in innovative solar and battery technologies, and in lighter and stronger construction materials. New classes of materials are currently at the edge of technological development. These classes include metamaterials, artificially architectured materials designed to have material properties beyond those of the individual components. Another class are active materials that are at the boundary between materials and devices, e.g. new biomedical soft materials which can autonomously perform sensor functions. A recent report commissioned by the German Environment Agency identified eight clusters of advanced materials (Giese et al., 2020), ranging from (DNA-based) biopolymers (Oomen et al., 2019) to advanced alloys comprising two or more constituents (Giese et al., 2020), whereas advanced materials in the Netherlands were categorized

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according to the main area in which the materials are applied (MaterialenNL Platform, 2020).

Novel materials with intricate structures can, however, impose new risks during their life cycle, e.g. exhibiting hitherto unobserved toxicity profiles or releasing nano-sized building blocks. Innovation processes would benefit from identification of potential health issues and environmental issues from early stages of innovation onwards, including the whole life cycle (Soeteman-Hernandez et al., 2019). Towards this goal, sustainable use of raw materials, and sustainable production, manufacture, use and recycling of the novel materials should also be considered. New applications of existing materials/substances due to new technologies or new manufacturing processes which can lead to new use pattern and consequently possible new risks, are also to be considered. To keep up with the pace of innovation foreseen within the European GD, it is therefore essential that appropriate risk governance is put in place that is capable of coping with the potential new risks and sustainability issues. National and international innovation policies therefore need to focus not only on the promotion of technology development, but should also include the development of appropriate risk governance that can keep up with innovations (Soeteman-Hernández et al., 2021). In light of lessons learned from the past of the nanotechnology domain, lack of such a balance can result in a situation of continued uncertainty amongst innovators and other stakeholders about the safety of materials, products and production processes, and about how to comply with legislation. The lack of a synchronized approach has led to risk governance that is increasingly lagging behind innovation, as is exemplified for nanomaterials (van Teunenbroek et al., 2017; Soeteman-Hernandez et al., 2019).

With the objective of a climate neutral and circular economy, we are now entering a new era in technical innovation that is focussed on the design of (amongst others) materials for tomorrow, also termed smart (nano)materials, advanced materials, or next-generation materials. In this paper we will use the term 'advanced material'. Advanced materials have in common that they are at the forefront of innovation with relatively little knowledge available on their potential adverse effects for man and the environment, as explained below. It is therefore of utmost importance to develop an anticipatory risk governance approach and to proactively avoid the occurrence of possible unexpected risks of these advanced materials, whilst not hindering innovation. Towards this goal, we propose a novel approach to systematically identify emerging issues of the materials of tomorrow. This approach can be applied by both regulators and innovators.

The goal of this systematic approach is the early identification of health, environmental and sustainability issues to support the Safe-and-Sustainable by Design (SSbD) development, production, use, and end-of-life treatment of advanced materials. This is important to fully exploit the innovation potential of advanced materials and to warrant that potential health, safety and sustainability issues are identified in an as early stage of development as possible. The approach is also aimed at creating trust amongst innovators and especially their customers that safety and sustainability aspects are properly considered from the initial stages of innovation. It is up to the users of the approach to decide on whether or not issues underlying sustainability (like social and economic aspects) are included in the prioritization that is the outcome of the framework. Furthermore it is to be noted that debate is ongoing on a proper definition of the term 'sustainability'. In this contribution we use the term 'sustainability' as used in the documentation underlying the European Green Deal (EC, 2019a).

Some considerations are given with regard to the design of the systematic approach, after which the various steps of the approach are presented. To exemplify the identification of emerging safety and sustainability issues of advanced materials, two case studies are presented. These case studies address materials that are fully different with regard to their composition, origin, and functionalities. The final part of the contribution deals with a discussion of the lessons learned from the case studies with regard to SSbD for advanced materials.

2. Background to the methodology for systematic identification of emerging safety and sustainability issues of advanced materials

The developed stepwise approach merges some aspects from the International Risk Governance Centre (IRGC) Guidelines for Emerging Risk Governance (IRGC, 2015) with some aspects from the EU Environmental Foresight System (EC, 2019b). The goals of the approach are:

i) to identify potential safety and sustainability issues and opportunities for specific advanced materials;
ii) for such identified signals, to gather information in a timely manner for informed decision-making on that specific material through the assessment of those issues that may develop into safety or sustainability issues in a timely manner;
iii) systematically compare signals to allow for prioritization and adaptive policy-making for risk governance.

These goals translate into a methodology that consists of the following steps:

1. Inventory of state of the art;
2. Sense making and prioritization;
3. Defining outcomes;
4. Evaluation and reflection.

2.1. Step 1: inventory of state of the art

This initial key step in an analysis to identify future safety and sustainability issues involves a general inventory of the latest developments within the broad field of innovative materials and innovative technologies, new applications of existing materials/substances due to new technologies or new manufacturing processes which can lead to new use pattern and consequently possible new risks, and consists of two activities:

1a) Scan the field to obtain an indication of the latest advancements in nanotechnology pertaining to advanced materials through periodic scanning of the scientific literature, news sites, websites, electronic databases and stakeholder networks. Recent events provide additional information and include for instance workshops such as e.g. The German Environment Agency Thematic Conferences on Advanced Materials (Dec. 2019, June 2020, Sept. 2020), and the EC Workshop on Safe and Sustainable Smart Nanomaterials (Sept. 2020). Other relevant sources include the European Technology Platform for Advanced Engineering Materials and Technologies (EuMaT). It is to be noted that this list is not exhaustive and needs to be updated on a regular basis.

1b) Narrowing the field. The field can be narrowed down by applying some pre-conditions which include basic considerations on: i) how close an advanced material/product is to the market and the potential scale of application; ii) whether the material/product has a significant societal or economic benefit; and iii) whether there are concerns on human health, legislation, sustainability, and/or economy.

2.2. Step 2: sense making and prioritization

Sense making and prioritization should be performed by a group of interdisciplinary experts covering the areas of physical chemical properties, ecotoxicity, environmental fate, human toxicity and sustainability. The following topics are to be addressed in more detail:

- functionality and application of material/product,
- safety assessment (human health and environment),

- regulatory frameworks,
- sustainability, and
- SSbD (fulfilment of policy ambitions).

For example, as part of the topic 'functionality and application of material', the Science–Technology–Application–Market (STAM) emergence framework is one way to get an indication on how close a material is to the market (Phaal et al., 2011). The STAM framework divides the industrial lifecycle into science, technology, application, and market phases and draws on demonstrators, such as commercial application demonstrators, to indicate transitions through these phases (Phaal et al., 2011; Featherston and O'Sullivan, 2017). This framework can be analogous to the Technology Readiness Levels (TRLs) which describe the technological development stages of the innovation process (EARTO, 2014). It is important to realize that the most effective options to best implement SSbD strategies are in the early innovation stages, as here modifications of the material (and also product) design in light of possible adverse risks and sustainability can be implemented at the lowest cost. At higher TRLs there is often simply no way back in this respect (Arvidsson et al., 2018; Jeswiet and Hauschild, 2005).

Each topic is broken down into more detailed sub-topics, as illustrated in Table 1. A distinction is to be made between clear and weaker indications on e.g. whether health or environmental risks are expected, or whether this is unknown or uncertain. Particularly in early stages of product development, data on material safety is scarce or even virtually lacking, which leads to higher uncertainty in expectations. At the end of step 2 the materials of highest concern are prioritized and passed on to step 3. It is to be noted that step 2 is a screening step and deals with an assessment that is based on expert knowledge and generally available information.

2.3. Step 3: defining outcomes of sense making and prioritization

From Step 2, the most crucial topics and possible actions can be identified, e.g. for functionality and (scale of) application of material, safety assessment (human health and environment), regulatory frameworks, sustainability, and SSbD (fulfilment of policy ambitions) (Table 2).

2.4. Step 4: evaluation and reflection

In this final step, the impact of the signals and the action(s) taken will be evaluated, reflected and monitored. This reflection step helps to preserve the overview of the field. It also helps to showcase the improvements made and learn from earlier actions. This enables full exploitation of the innovation capacity inherent in advanced materials whilst balancing possible adverse impacts. It is up to the evaluators of the systematic approach to decide on the depth of this step, the detailed (quantitative) nature of the information needed before taking a decision, and on the tools used for more in-depth evaluation. These tools may vary from a preliminary risk assessment to a preliminary LCA or sustainability assessment, although it is to be realized that for materials in their early stages of development, basic data may be lacking whereas also the actual applications may not be fully clear at this stage.

Table 1
An overview of topics and sub-topics that are relevant for 'sense making and prioritisation'.

Topic	Sub-topic
Functionality and application	• On market or close to market • Scale of application
Safety assessment human health	• Physico-chemical properties • Hazard • Kinetics • Exposure
Safety assessment environment	• Physico-chemical properties • Hazard • Fate • Exposure
Applicability of regulatory frameworks	• Identification of relevant regulatory frameworks (including applicability assessment of underlying test methods and assessment strategies)
Sustainability	• Raw materials • Manufacturing and production • Use • End-of life (recyclability and reusability / waste)
Safe and sustainable by design	• Safe and sustainable by design during innovation process

Table 2
General overview of the possible actions in relation to each topic, as examples of possible risk-governance-related actions identified in an adaptive policy-making approach.

Topic	Possible actions
Functionality and application	- Obtain more information on how close the material is to the market, the potential scale of application and whether the material has a significant societal or economic benefit (including the issue of essential use, as advocated by the European Commission in its chemicals strategy (EC, 2020) - Gather detailed information of (anticipated) applications
Safety assessment (human health and environment)	- Reduce uncertainties by generating (safety) data - Encourage development of suitable (standardized) test methods - Develop guidance, best practices
Regulatory frameworks	- Increase the preparedness of regulators for dealing with emerging safety and sustainability issues by sharing knowledge with the relevant Agencies, Authorities and Committees (EMA, ECHA, EFSA, SCCS[a]) to allow timely consideration that safety and sustainability issues of advanced materials are covered in the current regulatory frameworks - Define guidance, best practices - Encourage development of suitable (standardized) test methods
Sustainability	- Identify areas of relevance to sustainability, e.g.: • Reduction of environmental impacts (e.g. global warming potential by reduction of greenhouse gases) • Minimization of raw material use • Effective recyclability and reusability
SSbD (Fulfilment of policy ambitions)	- Encourage SSbD, Circular Economy, recyclability – provided that the Circular Economy and recyclability are environmentally sustainable. - Facilitate interaction between relevant stakeholders
General	- Monitor developments

[a] EMA, European Medicines Agency; ECHA, European Chemicals Agency; EFSA, European Food Safety Authority; SCCS, Scientific Committee on Consumer Safety.

3. Towards implementation of the methodology for systematic identification of emerging safety and sustainability issues of advanced materials

Actual implementation of the proposed methodology requires gaining experience in the operationalization of each of the steps proposed. Step 1 is to be initiated by a general scan of the field, ideally performed on a regular basis. Subsequently, step 2 is performed in collaboration with policy makers by a team of interdisciplinary experts. The outcomes of step 2 are further elaborated in step 3. Typically, additional information is gathered in this step to allow deciding on whether or not further action is needed. The impact of the actions taken is put in a broader perspective in the reflective step 4, in which the innovation capacity is balanced with possible adverse impacts.

To illustrate the considerations that constitute an essential part of step 2, two case studies were performed on classes of materials that are considered critical within the aim of reaching some of the transitions and goals of the European GD. The case studies were selected to exemplify the typical issues encountered when dealing with novel materials, such as lack of data, uncertainty about the stage of innovation, scale of application and other information available, imbalance of the types of information that are crucial in balancing innovative capacity and safety. The first case study focuses on next-generation multifunctional carbon-metal based nanohybrids. Combinations of carbon nanomaterials (e.g., carbon nanotubes, functionalized graphene family nanomaterials, carbon dots, and graphitic carbon nitride) and metal(oxide) nanoparticles are the most commonly pursued nanohybrids. They exhibit appealing novel properties and multifunctionalities that have the potential of solving various complex challenges, e.g. those faced in the transition to a green energy-based society. The second case study deals with functionalized cellulose composite nanomaterials (CNM). This case study is triggered by the fact that cellulose nanomaterials are a class of nature-based renewable materials that have recently garnered attention in various fields, including structural materials, biomaterials, construction, paper enhancement, and others. Cellulose is a nanosized component of wood that gives wood its mechanical properties, and cellulose nanomaterials are thus strong and stiff. Moreover, they are biodegradable and sustainable, and are a huge resource (used in the order of gigaton yr^{-1}) (Shatkin and Kim, 2015).

4. Case study 1: next-generation multifunctional carbon-metal based nanohybrids

This case study presents the application of multifunctional carbon-based nanohybrids in energy related applications in which carbon-based nanomaterials are combined with metallic or metal oxide nanoparticles. The case study was selected because of the current societal relevance of innovations within the energy sector that range from energy harvesting to energy storage, combined with the potential advantages offered by nanohybrids in these innovations (Pomerantseva et al., 2019; Wang et al., 2019).

4.1. Functionality and application

Combining different nanomaterials at the nanoscale enables innovations that are of use within the transition of the energy sector towards more sustainable energy provision. Examples include the more efficient capture of solar energy, more efficient generation of hydrogen as an alternative power source, and advanced systems for energy storage (Wang et al., 2019). Typically, carbon nanomaterials such as carbon nanotubes, (modified) graphene, or graphitic carbon nitrides are combined with metallic or metal oxide nanoparticles in these innovations. This yields hybrid or composed materials that are also suited to act as catalysts in the production of alternative energy, such as in the conversion of CO_2 into fuels like methane and methanol.

These nanohybrids are currently in their early stages of development and the principal underlying processes have been assessed, e.g. the improved efficiency of capture of solar energy. It is broadly recognized that the potential benefits of hybrid nanomaterials in the transition towards green energy are enormous, but it needs to be realized that the concept is not yet operational at a large scale (Wang et al., 2019). All examples found are therefore currently in between TRLs 1 and 3, i.e. reaching the stages of prototyping and incubation. The proof of concept (TRL 3) has been provided for the specific applications of splitting water into hydrogen and oxygen, and the transformation of CO_2 in energy carriers like methane and methanol (Wang et al., 2019). Nevertheless, the basic knowledge on the exact catalytic performance of the nanohybrids in these applications is still limited. A limited number of hybrid materials, such as a silica-carbon hybrid in electrolysis, are currently commercially applied, although at a small scale (Wang et al., 2019). It is not possible yet to predict which applications of carbon-metal(oxide) nanohybrids will reach the highest TRLs of large-scale industrial application, but based on the considerable efforts industry is investing their development, it is reasonable to assume that some of the applications currently in development will indeed proceed to market scale. This is in line with the general development that only a fraction of promising novel materials and technologies finally reach the market.

4.2. Safety assessment: human health and environment

The key question in assessing the impact of hybrid materials on human health and the environment, is whether the overall impact of the hybrid material exceeds the sum of the impacts of the individual constituents. This might for instance be the case when specific interactions between the individual constituents making up the hybrid yield reactive intermediates, either in the exposure phase or after interactions with biota, resulting in cellular uptake. Linked to this option, it is also possible that new functionalities induce adverse effects that were not identified before for the individual components. An example is the possible formation of internal electromagnetic or electrical fields in the composite material. Knowledge on potential hazardous impacts of such novel properties is virtually absent. In addition, the option of hybrid materials increasingly yielding reactive breakdown products has so far remained unexplored. Such reactive breakdown products might induce tissue damage, which could become irreversible leading to e.g. fibrosis, or they might cause DNA-damage, which subsequently might induce tumour formation. Furthermore, the distribution of a hybrid material in either the environment or in the human body may differ substantially from the distribution of the individual components. This may cause impacts of hybrids at other sites of toxicity within the body than the target sites for the individual constituents. Taken together, this information implies that issues that might arise with regard to safety for man and the environment due to the novel hybrids cannot be predicted on the basis of the known impacts of the individual components.

4.3. Applicability of regulatory frameworks

Some applications of hybrid materials in the energy sector are expected to be in electronic devices. European legislation applicable to electronic devices includes:

- The Waste of Electrical and Electronic Equipment Directive of the European Commission (EC, 2003), aimed at recycling and reuse of electronics with a focus on ease of reuse of electronics and electronic components and the collection of electrical devices by consumers.
- The European Union Directive on the restriction of the use of certain hazardous substances in electrical and electronic equipment (EU, 2011) limits the use of some hazardous substances in electronics. Amongst others, maximum concentrations of hazardous substances such as lead, mercury, cadmium, chromium(VI) and some brominated flame retardants have been prescribed and there is the requirement of substitution of these hazardous substances by safer and more sustainable alternatives.

Harvesting of solar energy is not addressed by these directives, and for this specific application, it is likely that at higher TRLs, the hybrid materials used will be regulated through application of the overarching REACH legislation (EC, 2006). REACH requires producers to assess the risks of the newly developed hybrid materials to human health and the environment when they are placed on the EU market. The way a (hybrid) material is dealt with within REACH – for instance as a substance, a mixture, a nanomaterial (nanoform), or a so-called article – together with the level of the production or importation tonnage determines the information requirements for the material. For instance, in case of substances in an article, the information to be submitted depends on possible human or environmental exposure, concentration and other factors. REACH requires separate registration and safety assessment of each of the substances of a mixture. It thus cannot be excluded that the possible synergistic or antagonistic effects of a mixture are either overlooked or underestimated under this regulation.

In case of TRL exceeding 7 (i.e. (pilot) plants), additional concerns related to worker and consumer safety need to be addressed. Fortunately, materials used in applications within the energy sector are often enclosed within the devices/products, e.g. in the case of solar panels. This implies limited exposure of consumers. Also, closed production systems can help to ensure worker safety.

4.4. Sustainability

Various considerations apply when considering the sustainability of nanohybrids. First of all, it should be realized that the hybrids are being developed for a tailored application for which the costs, in terms of for instance energy and resource-efficient materials use, need to be balanced by the benefits in sustainable applications such as energy harvesting and photocatalysis. On the other hand, the hybrid nature of the materials and the tailored design reduce the options for recycling materials and re-using the hybrids. Recycling with the aim of retrieving valuable materials, e.g. noble and rare elements, is often accompanied by high energy input or use of harmful extractants such as strong acids. This too might negatively affect the sustainability balance, and a careful selection of suitable end-of-life approaches is essential in this respect.

4.5. Safe and sustainable by design

Safety considerations are a precondition for widespread application of innovative materials. Yet, based on the currently publicly available information, attention seems to be mainly focused on the technical perspectives of several kinds of nanohybrid materials, with little attention paid to issues like safe-by-design or considerations of alternative materials to improve material safety. In this respect, the lack of knowledge on materials safety is currently the main source of uncertainty, rather than the lack of consideration of alternative materials per se. Especially the consideration of issues such as reuse of materials and possible impacts on human health and the environment during the production, use and waste stages of the materials is still in its infancy. In this respect, the general rule is that the more complex the composition of a material, the more complex it will be to recycle the individual components. Given that the various components of a hybrid material are closely intertwined, recycling is likely to be a complex issue.

5. Case study 2: nanocellulose composites

This case study deals with the use of nanocellulose as part of composite materials designed for use as construction materials. In contrast to the materials used in the first case study, cellulose nanomaterials are nature-based renewable materials that are quickly gaining ground, amongst other reasons within the drive towards a sustainable circular economy. Composite construction materials based on nanocellulose benefit from the mechanical properties of cellulose, also enhanced by various kinds of polymers. An additional consideration for the selection of this case study is related to the common misperception that nature-based materials are by definition harmless to human health and the environment.

5.1. Functionality and application

Cellulose is a biopolymer known for its high mechanical strength. It is available in large quantities, e.g. from natural sources or paper recycling. Cellulose nanomaterials (CNMs) can be produced by mechanical or chemical treatment of cellulose, and have at least one dimension that is smaller than 100 nm. CNMs have been applied since roughly 1992, but applications are strongly increasing, especially in the last five years. This increase can be attributed to their low cost, and their perceived “green” (renewable, sustainable) nature which is increasingly important in the context of the circular economy (Clarkson et al., 2020). CNMs are inherently incompatible with most man-made materials in use nowadays. In technical terms a key challenge is to combine hydrophilic CNMs with the typically hydrophobic constituents of nanocomposites (Clarkson et al., 2020). To take full advantage of the use of CNMs and compensate for the disadvantages, nanocomposites can be formed that combine CNMs with different types of other natural and/or synthetic polymers.

It should be noted that we are dealing with various kinds of nanocomposites with different performance characteristics and potential scales of application. Some composites are in an early stage of development, while others are already on the market, as reviewed recently by Sharma et al. (2019). Overall, some CNM-enabled products are on the market today, whereas most advanced nanocomposites are currently under development, as for instance illustrated by (Clarkson et al., 2020). Technical developments, partly triggered by extra efforts invested in ‘green chemistry’, speed up product development. CNM composites are increasingly obtaining properties comparable to existing ‘competitor’ materials. One example is the recent discovery that CNM composites have specific strength similar to that of aircraft aluminium (El Awad Azrak et al., 2019). More specifically, CNM thermoplastic nanocomposites have good toughness, and novel strategies are currently put in place to increase stiffness and strength to take advantage of their ease of processing and low density over materials such as metals in the automotive and aerospace industries.

5.2. Safety assessment: human health and environment

The potential safety issues of cellulose nanomaterials are diverse, and can be related to:

1. the (functionalized) CNMs themselves;
2. the toxicity due to release of other substances during preparation of the nanocomposites (the relevance of this issue depends on the process used);
3. the (combined) toxicity of the constituents in the actual nanocomposites, following production and including use, recycling, and waste stage.

The risks related to CNMs differ across the different life stages of the composites. Initially, the risks relate to the production of CNMs, the emissions and the hazards of the CNMs released. There are five main categories of cellulose nanomaterials that can be produced from cellulose sources: cellulose nanofibrils (CNFs), cellulose nanocrystals (CNCs), tunicate CNCs, algal cellulose, and bacterial cellulose (Clarkson et al., 2020). The CNMs differ in morphology (shape, size, aspect ratio), surface characteristics, function, production process, and use. CNFs and CNCs are the most frequently used materials in CNM composite research. Depending on the production process and the source material, CNCs have a general length of 15 μm, and a general width of 10–50 nm (Stoudmann et al., 2020). The flexible fibres of CNF have a width between 3 and 100 nm, are longer than 1 μm, and can form web-like structures. They are generally less rigid than CNCs. Amongst other things, the size and rigidity of the fibres need to be considered as related to possible specific inhalation hazards. Thereupon, the impact of functionalization of the nanomaterials on possible hazards to man and the environment needs to be assessed, as functionalization may not only significantly affect the functionality but also alter the toxicity profile of the materials.

The characteristics of the CNMs affect the way they are processed into the final nanocomposite, which in turn affects the characteristics of the nanocomposite (Tu et al., 2020; Clarkson et al., 2020). Safety issues for human health and the environment may emerge due to release of substances during preparation of CNMs and nanocomposites, or due to the combined toxicity of the constituents in the actual nanocomposites. These are potential risks during production, but also during use, recycling, and waste stages.

A recent review by Stoudmann et al. (2020) elucidates existing knowledge and knowledge gaps on the human health hazards of cellulose nanomaterials. Few studies have focused on the toxicity of CNMs. Moreover, results are often incomparable, due to differences in tested materials and the methods used. Stoudmann et al. (2020) conclude that exposure to CNMs through inhalation may affect human health. On the other hand, dermal contact in an occupational setting likely poses a low risk. In general, there is a lack of long-term studies on pulmonary exposure, biopersistence, long-term dermal exposure (from e.g. wound dressing), and effects of surface modification. In addition, studies should focus on inflammation, especially in the context of the fibre paradigm (Stoudmann et al., 2020). Shatkin and Kim (2015) identified an additional data gap, which is consumer exposure to CNMs through e.g. food packaging. Some of these gaps for unmodified CNCs have been recently addressed, including a 90-day rodent feeding study (Ede et al., 2020). An additional publication (Stoudmann et al., 2019) predicts a low environmental risk from CNMs in surface water, although local concentrations have not been considered due to scarcity of production information.

Extensive options exist for composing different CNM-based nanocomposites with an enormous variety of properties and technical functionalities. It is therefore difficult to make generalized conclusions regarding the toxicity of nanocomposites. Regardless, it should be kept in mind that human and environmental exposure is likely to increase with the increasing applications of CNMs. In addition, it is to be noted that the fact that parts of the CNMs are of natural origin is not a sound argument for waiving hazard assessment.

5.3. Applicability of regulatory frameworks

It is up for discussion if current regulatory frameworks adequately cover CNM and CNM-based nanocomposites. Generally, the regulatory frameworks are judged as being able to cope with nanocomposites; terminology is sufficient for identifying the materials, and in principle it is possible to collect the data needed for proper risk assessment.

Pragmatic problems for regulatory frameworks might be related to the wide variety of possible nanocomposites and surface modifications, in terms of types of nanocellulose used, and the extensive options for composing different CNM-based nanocomposites with an enormous variety of properties and technical functionalities. At this moment, 180 cellulose types are registered under the EU REACH regulation. It should be noted that cellulose pulp is specifically exempted from obligation to register under REACH on the list in Annex IV.

As emphasized by Clarkson et al. (2020), one should pay close attention to the characteristics of the CNMs when comparing study results. Some guidance exists on characterization of CNFs and CNCs (Foster et al., 2018), although standardized test methods and general guidance on characterization of CNMs are lacking.

5.4. Sustainability

In theory, the market for CNMs is infinite in the sense that a virtually infinite pool of raw material (cellulose) is available and continuously being replenished. There may however be sustainability issues in the production processes, e.g. in energy use. It should be pointed out that for the specific application of CNM-based nanocomposites, the non-CNM part is often not 'green' and is considered to be non-sustainable. Examples include butadiene rubber, epoxy resins, polyurethane, and polyacrylonitrile.

5.5. Safe and sustainable by design

Studies concerning safe (and sustainable) by design or life cycle assessment considerations of CNMs are scarce. As acknowledged by Shatkin and Kim (2015), now is the time to address safety concerns because production of CNMs is mostly at the pilot stage. It should be noted that LCA considerations are likely to be relevant, as the nature of the materials/products/ applications changes over time: cellulose is transformed into nanocellulose and nanocellulose subsequently combined with other materials to form nanocomposites. These composites are subsequently used, recycled, and becoming waste.

In terms of circular economy, parts of the composites are by definition of natural origin, and cellulose-based materials are commonly recycled. However, as already indicated above for the case of nanohybrids, as a general rule the more structurally complex the material, the more difficult it is to recycle unless for use in similar applications. In this specific case it should be noted that in most applications of CNM-based nanocomposites, it is by definition not possible to recycle the individual components. This will generally limit the available recycling options to uses in similar applications.

6. Evaluation and reflection

The examples described here of carbon-metal hybrid materials for the specific application in the energy sector and nanocellulose in various applications show that a quick screening efficiently highlights some concerns on safety and sustainability. The (expected) scope of use and the information about the applicability of current legal frameworks help to put issues of interest into perspective.

With the information generated by means of the systematic approach, as described in this contribution, decisions can be made on potential actions. First of all, certain sectors or companies can be encouraged to apply the principles of 'safe and sustainable by design'. Within 'safe and sustainable by design', the focus during the innovation process is not merely on functionality, as possible risks to human health and the environment and sustainability concerns are also explicitly considered in the product and the process design (Jiménez et al., 2020). This may initiate further research in the optimization of the balance between product functionality and safety. In addition, the relevant legislation should be clarified as early in the design stage as possible, including information on how the various international guidance documents deal with novel materials. In case of uncertainty on how legislation addresses certain issues related to the novel materials, there is opportunity for timely discussions and clarification. Targeted scientific research can also be performed. As an example, in the specific case of carbon-metal nanohybrids one could examine how the (joint) risk profile of the various components of the hybrid materials can be taken into account as balanced by the technical performance of the hybrid material. An issue of specific interest for the case of these hybrid materials relates to the possible biological impacts of novel properties, such as an internal electromagnetic field or an electric field within a hybrid material. Also the behaviour of the material after absorption by an organism is a topic of possible concern. On top of this, the case study of nanocellulose flags the issue that despite the basic material being 'green' by definition, sustainability difficulties are likely to arise e.g. during the waste and recycling stages. In most applications of CNM-based nanocomposites, it is not possible to recycle the individual components.

The examples of innovative composite materials discussed here are at an early stage of development (TRL 1–3). The rate at which innovations enter the market varies enormously. It is therefore not possible predict when such materials could actually reach the market, if they do at all. Consequently, it is at this stage also not clear when it is best to decide on possible follow-up activities or on specific actions. The lower the TRL level, the more unlikely it is for an innovation to finally reach the market. On the other hand: at high TRL levels there are fewer options for making changes. Increasing the safety or sustainability by modification of either the newly developed material or of the process design is then more difficult in common practice. This might be described as the design paradox, balancing the many degrees of freedom in the early development of a technology or of a novel product (Arvidsson et al., 2018) with the fact that about 70% of the final costs and impacts on the environment originate from decisions made in the early phase of research and development of a technology (Jeswiet and Hauschild, 2005).

The various aspects of the systematic approach have been viewed qualitatively in the current examples on the basis of several overview publications. How the various aspects can be viewed systematically and more quantitatively is to be further elaborated. This can for instance be done on the basis of questions such as:

- How can the (expected) market size be more accurately estimated?
- How can the proximity to the market and the progress of innovations be monitored?
- How can hitherto unknown hazards (hazard mechanisms) be taken into account?
- How to quantify sustainability of materials and products?
- How to optimize the awareness of innovators of potentially relevant regulations and guidelines?

By carrying out this exercise for other novel materials as well, the consideration of possible actions can be viewed more widely. This makes it possible to work more systematically on the development of new, safe and sustainable materials. It is therefore important to consider how new material groups can be efficiently identified within step 1 of the framework presented here.

7. Outlook for the strategic approach

Various aspects of the approach for identification of emerging safety and sustainability issues of advanced materials have been highlighted above. After the identification of specific cases, several follow-up activities can be foreseen to extend and implement the methodology in practice for the specific cases. These activities are case-specific and include:

- Monitoring developments. This refers to technological developments as well as politically driven trends, including potential consequences to for instance the Green Deal.
- Encouraging development of suitable, standardized, test methods – as currently developed within ISO and OECD for fate and hazard assessment of nanomaterials.
- Generating the required (safety) data.
- Gaining insight from materials science – couple this approach to the knowledge available from the materials sciences.
- Facilitating SSbD, sustainability, LCA, recyclability: weighing of economic and societal benefits versus ‘costs’, and raise awareness of the need to consider the whole life cycle of a material and its benefits versus adverse impacts.
- Facilitating interaction with relevant stakeholders: innovators, policy makers, (regulatory) risk assessors.
- Considering the issue of essential use as advocated by the European Commission.
- Based on experiences when the system has further matured: transformation into a broadly accepted/supported scanning system for systematically prioritizing advanced materials at as early stages of innovation as possible.
- Development of guidance and best practices for testing safety and sustainability issues. Dependent on experience gained during the extension of the methodology, guidance should be developed on *ex ante* driven assessment of technologies and associated safety issues. Execution of additional case studies serves the purpose of defining best practices and defining key issues of focus.

The simultaneous development of guidance, the preparation of an overview of best practices and the further extension of the systematic approach proposed in this contribution, can serve as a blueprint for weighing the costs and benefits of other key issues that are central in achieving the European goal of a sustainable climate neutral and circular economy by 2050. It is also important to note that the proposed methodology can feed into or use information from the new ‘Advanced Technologies for Industry’ platform that is currently under design. The Advanced Technologies for Industry (ATI; ati.ec.europa.eu) project deals with the implementation of the EU's industrial policy approach which promotes the creation of a competitive European industry. The ATI project has been set up to support the implementation of the associated policies and initiatives, and to set up a systematic monitoring of technological trends and to generate reliable, up-to-date data on advanced technologies. Information on and balancing of safety aspects would effectively complement the ATI platform.

Finally, it should be noted that the systematic approach proposed here is of potential benefit to both innovators and regulators in the broadest sense: at an early stage of development of their advanced materials, innovators will be made aware of possible hitherto unforeseen hazards associated with these materials. Furthermore, the approach allows regulators to ask the right questions regarding the potential (future) environmental and human health impacts of emerging innovations, i.e. it allows for regulatory preparedness. The tool to be developed in the future in support of the framework is above all intended to create awareness, to be followed by joint activities of all stakeholders aimed at the actual implementation of the safe and sustainable design of advanced materials.

Credit author statement

All authors contributed equally to the preparation of the manuscript.

Declaration of Competing Interest

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

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