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Risk Governance of Advanced Materials

Considerations from the joint perspective of the German Higher Federal Authorities BAuA, BfR and UBA

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Preface: Risk Governance of Advanced Materials

This document summarises the current activities, considerations and recommendations of the German Environment Agency (UBA), the German Federal Institute for Risk Assessment (BfR) and the Federal Institute for Occupational Safety and Health (BAuA) aiming to establish good governance of advanced materials (AdMat) to ensure their responsible development, use and recycling considering human and environment safety. It builts on the joint research strategy on application safety and environmental compatibility of nanomaterials (NMs) and other AdMat (BAuA et al. 2016) and also considers the discussions during numerous events such as, e.g. the NanoDialogue conducted by the Federal Ministry of the Environment, Nature Conservation and Nuclear Safety (BMU). Importantly, many of the issues addressed for NMs[1] also apply to more complex AdMat.

The document starts with setting the scene and pointing out relevant linkages of the topic to overarching strategies and goals for chemical safety on the European and international level. It is followed by a working definition of "advanced materials", which is intended only to facilitate a targeted discussion of the thematic field. It is explicitly not intended as a basis for regulation of AdMat. For the purpose of systematically identifying those materials that give rise for concerns, a definition of "Materials of Concern" is proposed and it is shown how these - in cooperation with relevant stakeholders - can be identified and assessed at an early stage. For this purpose procedures and criteria are described that are currently being elaborated in an German Interagency Working Group under the leadership of the BfR. Next, challenges with respect to "regulatory preparedness" are discussed highlighting the need to continuously adapt existing legislation and regulations to keep pace with innovation. To this end, the novel concept of "Regulatory Readiness Levels" is introduced to facilitate policy advice and enabling targeted funding for applied research. Recommendations for the safe and sustainable design of AdMat and on the necessary knowledge transfer to developers and manufacturers are addressed. Building on the joint research strategy, needs for future research are identified. In a concluding chapter, examples of AdMat are given, which the involved higher federal authorities are currently dealing with intensively: advanced polymers, additive manufacturing, respirable fibres, nanocarrier as well as active and intelligent packaging. These examples also illustrate the high level of complexity in the world of AdMat. The document closes with a summary of the main conclusions und recommendations.

This document was developed in the framework of a departmental research project on AdMat and their implication for chemical safety funded by BMU[2] to provide a framework for stakeholders to discuss challenges posed by AdMat at the final of three thematic conferences on "Advanced Materials - Identification of Governance Needs" organised by UBA on 14 June 2021.

This document is intended to serve as thought starter for further in-depth discussions. It is anticipated that with increasing investigation of challenges and needs for actions as well as progressing governance activities on AdMat the presented perspectives or parts of it will need to be updated and/or deepened. Therefore, comments on the presented framework to promote the discussion and to further substantiate the efforts needed for a good governance of AdMat are welcome in the course of future exchange and cooperation.

[1] limited to a size range of 1 – 100 nm according to the European Commission (2011): Recommendation on the definition of a nanomaterial (2011/696/EU) https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32011H0696

[2] ReFoPlan project FKZ 3719 66 4020, results available at https://www.umweltbundesamt.de/publikationen/advanced-materials-overview-of-the-field-screening

Vorwort: Risikogovernance von neuartigen Materialien: Die Risiken von neuartigen Materialien sachgerecht kontrollieren

Dieses Papier fasst die aktuellen Aktivitäten, Überlegungen und Empfehlungen des Umweltbundesamtes (UBA), des Bundesinstituts für Risikobewertung (BfR) und der Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA) zusammen, die darauf abzielen, eine sachgerechte Risikogovernance von neuartigen Materialien (AdMat) zu etablieren, um deren verantwortungsvolle Entwicklung, Verwendung und Recycling unter Berücksichtigung der Sicherheit von Mensch und Umwelt zu gewährleisten. Es baut auf der gemeinsamen Forschungsstrategie zur Anwendungssicherheit und Umweltverträglichkeit von Nanomaterialien und andere innovative Werkstoffe (BAuA et al. 2016) sowie den Diskussionen bei zahlreichen Veranstaltungen wie z.B. dem NanoDialog des Bundesministeriums für Umwelt, Naturschutz und Reaktorsicherheit (BMU) auf. Wichtig ist, dass viele der für Nanomaterialien angesprochenen Themen auch für komplexer aufgebaute AdMat gelten[3].

Das Papier beginnt damit, den Rahmen abzustecken und relevante Verknüpfungen des Themas mit übergreifenden Strategien und Zielen zur Chemikaliensicherheit auf europäischer und internationaler Ebene aufzuzeigen. Es folgt eine Arbeitsdefinition von "Advanced Materials" (neuartige Materialien), die eine gezielte Auseinandersetzung mit dem Themenfeld ermöglichen soll. Diese ist ausdrücklich nicht als Grundlage für eine Regulierung von AdMat gedacht. Zur systematischen Identifizierung von besorgniserregenden Materialien wird eine Definition von "Materials of Concern" (bedenkliche Materialien) vorgeschlagen und aufgezeigt, wie diese - in Zusammenarbeit mit relevanten Stakeholdern - frühzeitig identifiziert und eingeschätzt werden können. Dazu werden Verfahren und Kriterien beschrieben, die derzeit in einer deutschen behördenübergreifenden Arbeitsgruppe unter Federführung des BfR erarbeitet werden. Im Folgenden werden Herausforderungen im Hinblick auf die "Regulatory Preparedness" (regulatorisches Vorbereitetsein) diskutiert, wobei die Notwendigkeit einer kontinuierlichen Anpassung bestehender Gesetze und Verordnungen an die Geschwindigkeit von Innovation herausgestellt wird. Zu diesem Zweck wird das Konzept der "Regulatory Readiness Levels" (Grad der regulatorischen Reife) vorgestellt, um die Politikberatung zu erleichtern und eine gezielte Förderung der angewandten Forschung zu ermöglichen. Empfehlungen zur sicheren und nachhaltigen Gestaltung von AdMat und zum notwendigen Wissenstransfer an Entwickler*innen und Hersteller*innen werden angesprochen. Aufbauend auf der gemeinsamen Forschungsstrategie wird der Bedarf für zukünftige Forschung aufgezeigt. In einem abschließenden Kapitel werden Beispiele für AdMat genannt, mit denen sich die beteiligten Bundesoberbehörden derzeit intensiv beschäftigen: neuartige Polymere, additive Fertigung, lungengängige Fasern, Nanocarrier sowie aktive und intelligente Verpackungen. Diese Beispiele verdeutlichen auch die hohe Komplexität in der Welt der AdMat. Das Papier schließt mit einer Zusammenfassung der wichtigsten Schlussfolgerungen und Empfehlungen.

Das vorliegende Dokument Papier wurde im Rahmen eines vom BMU geförderten Ressortforschungsprojekts zu AdMat und deren Auswirkungen auf die Chemikaliensicherheit[4] entwickelt, um einen Rahmen für die Diskussionen mit Stakeholdern für die finale von drei Themenkonferenzen zu "Advanced Materials - Identification of Governance Needs" am 14. Juni 2021 zu bieten.

Dieses Papier soll als Denkanstoß für weitere, vertiefende Diskussionen dienen. Es wird erwartet, dass mit zunehmender Untersuchung der Herausforderungen und des Handlungsbedarfs sowie mit fortschreitenden Aktivitäten zu Risikomanagementsystemen für

[3] begrenzt auf einen Größenbereich von 1-100 nm gemäß EC (2011): Recommendation on the definition of a nanomaterial (2011/696/EU) https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32011H0696
[4] ReFoPlan Projekt FKZ 3719 66 4020, Ergebnisse verfügbar unter https://www.umweltbundesamt.de/publikationen/advanced-materials-overview-of-the-field-screening

AdMat eine Fortschreibung und Konkretisierung des vorgestellten Rahmens oder Teile davon erforderlich sein wird. Daher sind Kommentare zum vorgestellten Rahmen, die die Diskussionen voranbringen und die benötigten Bemühungen für eine sachgerechte Risikogovernance von AdMat konkretisieren, im Zuge von zukünftigem Austausch und Kooperationen willkommen.

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AdMat	Advanced materials
AOP	Adverse outcome pathway
BAuA	Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (German Federal Institute for Occupational Safety and Health)
BfR	Bundesinstitut für Risikobewertung (German Federal Institute for Risk Assessment)
BMBF	Bundesministerium für Bildung und Forschung (Federal Ministry of Education and Research)
BMU	Bundesministerium für Umwelt, Naturschutz und nukleare Sicherheit (Federal Ministry of the Environment, Nature Conservation and Nuclear Safety)
CAD	Chemical Agents Directive 98/24/EC
CEN	European Committee for Standardization
CLP	Regulation on classification, labelling and packaging of substances and mixtures (EC 1272/2008)
CMD	Carcinogen and Mutagen Directive 2004/37/EC
DaNa	Data on new, innovative and application-safe materials
DNA	Deoxyribonucleic acid
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EU	European Union
GBP	Granular biopersistent particles
IATA	Integrated approaches of testing and assessment
ISC3	International Sustainable Chemistry Collaborative Centre
ISO	International organization for standardization
JRC	Joint research centre
LCA	Life cycle analysis
MoC	Material of concern
MWCNT	Multi-walled Carbon Nanotubes
NESSI	Novelty, exposure, severity, scope, immediacy
NGO	Nongovernmental organisation

NMEG	Nanomaterial Expert Group (at ECHA)
OECD	Organisation for Economic Co-operation and Development
PARC	European Partnership on Assessment of Risk of Chemicals
PBT	Persistent, bioaccumulative, toxic
PLC	Polymers of low concern
PRR	Polymers requiring registration
REACH	Regulation for registration, evaluation and authorisation of chemicals (EC 1907/2006)
RMOA	Risk management options analysis
RNA	Ribonucleic acid
RRL	Regulatory readiness level
SbD	Safe(r) by design
SCCS	Scientific committee on consumer safety
SME	Small and medium enterprises
SPINE	Safe(r) by design policy international network
SSbD	Safe and sustainable by design
SUBSPORTplus	Substitution support portal (of BAuA)
SVHC	Substance of very high concern
TRL	Technology readiness level
UBA	Umweltbundesamt (German Environment Agency)
UN SDG	Sustainable Development goals of the United Nations
vPvB	Very persistent, very bioaccumulative
WPMN	Working Party on Manufactured Nanomaterials

1 Advanced Materials: Challenges for risk assessment, sustainability and governance

Printable electronics, lightweight components for cars or nanocarrier systems for medicine, cosmetics, and food – these innovative functional materials are known as examples of "Advanced materials" (AdMat). AdMat have special properties at atomic or molecular level and bear great potential for application in various sectors such as renewable energy, e-mobility, digitalisation, health care or conservation of resources. Thus, AdMat and innovative manufacturing processes are in the focus of current research and innovation, with anticipated benefits for the economy, the society and the environment (BMBF 2015; Horizon Europe[5]). The term covers a wide range of existing and emerging materials that demonstrate improved performance over traditional materials. Further examples are nanomaterials with special electrical or optical properties or biomaterials for cell culturing or drug delivery. This differentiates AdMat from "conventional materials", such as metal, plastic and concrete in their traditional uses.

The first challenge with respect to AdMat is that this term addresses materials with new or enhanced properties (compared to conventional materials). Therefore, **the term is subject to a time component**, meaning what is considered "advanced" today might well be considered "conventional" tomorrow. **The second challenge is that AdMat comprise a large variety of material types** with very different structures, properties and functionalities, **hampering a common understanding what AdMat actually comprise.** For the purpose of this document, AdMat should be understood as „materials that are rationally designed through the precise control of their composition and internal or external structure in order to fulfil new functional requirements "[6].

In its Chemical Strategy for Sustainability (European Commission 2020a), the European Commission stated to support the research and development of AdMat in various sectors „to deliver the green and digital transition". However, AdMat can only be considered positive regarding their sustainability, if they provide a positive contribution to the European Green Deal and the corresponding EU Chemicals Strategy for Sustainability, i.e., if beside the benefits also the potential risks for man and environment are identified and appropriate measures for safe handling are taken. To ensure this, governance strategies have to be developed depending on the respective type of material. However, also beyond Europe, the development of sustainable materials and processes are key to achieve a sustainable society. The United Nations Sustainable Development Goals (SDGs – Agenda 2030) set an overall reference framework also for the advancement of material developments[7]. The SDGs comprise a number of targets for which AdMat may play an important role to achieve them. Therefore, it is significant to improvet the overall sustainability of materials along their whole life cycle. Only in this way can AdMat help to foster the transition to a sustainable society. Thus, *inter alia*, criteria and indicators have to be developed and agreed in order to contribute to a future-oriented sound management of all innovations including emerging material design with respect to safety and sustainability over the whole life cycle.

In addition, strategies have to be developed to identifiy (and thereby preferably avoid the development, the production and use of) materials that are of "concern" within the broad material universe. In this context, issues already identified decades ago for conventional chemicals are also of relevance for AdMat, e.g., the lack of appropriate information, missing

[5] European Commission Horizon Europe Cluster 4: https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/cluster-4-digital-industry-and-space_en
[6] This draft working definition is proposed in cooperation with the German Interagency Working Group on Advanced Materials
[7] United Nations Sustainable Development Goals: https://sdgs.un.org/goals

standard methods to assess safety, inappropriate test strategies for poorly soluble chemicals like biopersistent particles and fibres, lack of responsibilities of producers within Europe but also of importers to demonstrate the safety of their articles, weak points of interfaces of chemical legislation to other regulatory regimes like for waste management or occupational safety and health. A broad spectrum of regulatory options is conceivable for the risk management of AdMat. These range from "soft" regulation, such as voluntary agreements and commitments, to "hard" regulations, such as bans on placing on the market. In the transition from "soft" to "hard" regulation, intermediate stages can be taken into account, e.g., technical guidelines or standards. However, research to clarify and substantiate the scientific basis and collaboration between material developers and risk assessment experts are also of high importance. This is because it is precisely in the early developmental stages of material innovation where opportunities are biggest for safe and sustainable design. **Thus, a broader concept of innovation is needed, which besides technological process and economic realisation also incorporates ecological and societal benefits, and which involves all stakeholders. Such a concept of innovation maintains the precautionary principle and existing standards of protection. It is furthermore characterised by new developments that facilitate the transition to a sustainable society**.

Summary Chapter 1

AdMat come along with a high complexity in composition and structure as well as a broad field of potential applications. AdMat show a great potential to provide technical solutions for the most pressing global challenges we are facing today, e.g. shortage in resources, energy revolution, health care, and environmental pollution. In order to provide a positive contribution to the transition to a more sustainable society, beside the benefits of AdMat also their potential risks for human and environment have to be identified and appropriate measures for safe handling and use have to be established.

2 AdMat: A proposal for a working definition

In order to deal with AdMat, a description of the landscape is required which one one hand outlines the variety and complexity of the involved materials and on the other hand explains as precisely as possible the scope of a risk governance strategy. **Within this document AdMat are understood as „materials that are rationally designed through the precise control of their composition and internal or external structure in order to fulfil new functional requirements."** This broad working definition implies that AdMat cover very different and heterogenous material types, including all intentionally manufactured nanomaterials and nanoenabled products. To cope with the complexity, clustering or categorisation approaches are useful to get an overview and to identify and name the different classes and types of AdMat. Such a categorisation step can also support priorisation of AdMat for further investigation and identification of possible challenges regarding safety and sustainability at a later stage. In general, different categorisation schemes are possible, e.g., according to material classes, or application fields. For the purpose of this document we would like to refer to a categorisation scheme proposed by Giese et al. 2020, which is outlined below in Table 1.

The working definition of AdMa is explicitly not intended as a basis for fundamental regulation of AdMat or to be used in an existing regulation! Rather, it should allow to work out which regulations already apply for AdMat in the EU and thus, have to be considered, as well as to identify possible lacks in risk and safety regulation. Furthermore, such a working definition will support exchange and cooperation, e.g. on dedicated research needs.

Table 1: Proposed Cluster of Advanced Materials (taken from Giese et al. 2020)

Cluster of advanced materials	Sub-cluster, e.g.
Advanced Alloys	Intermetallic, shape memory, high entropy
Advanced Polymers	electro-active, self-repairing, co-polymers
Biopolymers	DNA-based, RNA-based, protein-based, sugar-based, lipid-based
Porous materials	microporous, mesoporous, macroporous
Particulate Systems	quantum dots, supra-particles, nanoflowers, graphene
Advanced Fibres	organic, carbon-based (incl. CNTS), inorganic (e.g. silica)
Composites	macroscopic, fibre-reinforced, particle-inforced, hybrid materials (combination of organic and inorganic materials)
Metamaterials	electromagnetic, acoustic

Summary Chapter 2

A proposed working definition for AdMat is: "Materials that are rationally designed through the precise control of their composition and internal or external structure in order to fulfil new functional requirements". The working definition of AdMat is explicitly not intended as a basis for fundamental regulation of AdMat or to be used in an existing regulation!

3 Current regulatory framework in the European Union

3.1 Overarching EU chemicals legislation

Two regulations build the heart of the European chemicals legislation and form a framework of legal principles for placing substances and mixtures on the EU market: the Regulation for Registration, Evaluation and Authorisation of Chemicals (**REACH**) (EC 2006) and the Regulation on Classification, Labelling and Packaging (**CLP**) (EC 2008a). Within these chemicals legislations, "substance" means a chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used. A "Mixture" consists of two or more substances, which are not considered additives or impurities. "Article" describes an object, which during production is given a special shape, surface or design, which determines its function to a greater degree than does its chemical composition.

According to the **CLP Regulation**, the manufacturer or importer of a substance or mixture is responsible for an adequate classification relating to its potential physical, health or environmental effects and a corresponding labelling and packaging. The main elements of the label are the hazard pictogram(s), a signal word (danger, warning), a hazard statement (H phrase(s)) and a precautionary statement (P phrase(s)). Labelling is the most important legal instrument to inform consumers and workers about hazardous properties of a chemical element, substance or mixture. For substances of particular concern, as well as for biocides and pesticides, legally binding harmonised classifications are set. All classifications of substances are published in the classification and labelling inventory of the European Chemical Agency (ECHA). Harmonised classifications are taken up into Annex VI of the CLP regulation.

The **REACH Regulation** governs the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). According to the principle of "no data - no market", a chemical substance with production quantities above one tonne per year may only be placed on the EU market if it is registered at the ECHA. The testing and information requirements associated with the obligation to register increase with the quantity marketed. More than 23,000 substances have been currently registered. "Nanoforms of a substance" have been additionally introduced into REACH in 2018, to clarify additional information needs taking into account the special properties of nanomaterials (EU 2018a). If essential data for a risk assessment are missing for a substance, these can be subsequently requested or generated using evaluation instruments, like dossier evaluation and substance evaluation. Substances identified as being of very high concern (SVHC), e.g., due to carcinogenic properties, might be subject to authorisation, meaning that only those applications are allowed for which safe use can be demonstrated or the socioeconomic benefit exeeds the risk. Targeted restrictions and conditions for placing on the market are also possible, for example the European ban on asbestos is also part of the REACH Regulation. A restriction may also cover articles and includes imported products (mixtures and articles). Nevertheless, only limited obligations apply for articles under REACH.

A definition for "material" is lacking in both regulations, but it is clear, that they cover materials, which fit to the definitions of "substance" and "mixture". But the distinction from "article" is often unclear and difficult to decide. For example, mineral wools with randomly orientated fibres are substances (with a harmonised classification), continuous fibres are mostly regarded as articles.

3.2 Sector-specific EU chemicals legislation

In addition to the overarching EU chemicals legislations REACH and CLP there is a huge number of sector-specific chemicals legislation in the EU[8]. Here we aim to mention only a few of them with no intention to give a complete overview.

Cosmetic products are regulated according to EC 1223/2009 (EC 2009a). A 'cosmetic product' means any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours. To comply with this regulation, manufacturers have to prepare a product safety report prior to placing a product on the market and notify their products via the EU Cosmetic Products Notification Portal (CPNP). The regulation identifies banned (annex II) and restricted substances (annex III) and provides positive lists for colorants (annex IV), preservatives (annex V) and UV-filters (annex VI). It prohibits placing cosmetic products on the EU market for which the final formulation, ingredients or combinations of ingredients, and/or finished products have been the subject of animal testing. It was the first legal framework to include a definition for nanomaterials, to clarify the information requirements for nanomaterials and to request a labelling of cosmetic products containing nanomaterials. Any intended use of nanomaterials in cosmetic products must be notified to the Commission at least six months prior to placing them on the market. The Commission may request a scientific opinion from the Scientific Committee on Consumer Safety (SCCS) on the safety of specific nanomaterials. The SCCS has also published a guidance document for risk assessment of nanomaterials in cosmetics (SCCS 2019). Currently, environmental risk assessment is not carried out under EU cosmetics regulation.

The **biocidal products** regulation (EU) 528/2012 (EU 2012) requires a two-step assessment procedure. Firstly, the active biocidal substances are approved at EU level and entered on a positive list for a time-limited period. Secondly, any products containing listed active substance(s) must be authorized either at Member State level by the national authority, or at EU level via ECHA. ECHA maintains an on-line register of all authorised biocidal products. This legislation also further specifies the conditions for classification, packaging and labelling of biocidal products, referring also to CLP. In general, data requirements address both, the active substances and the whole products and go beyond the dataset specified in REACH. The biocidal products regulation has also implemented a definition of nanomaterials and the notification, assessment and approval of the nanoscale form of an active substance must be carried out additionally to any potentially existing non-nanoscale form.

The approval and authorisation of **plant protection products** and their active substances, respectively, is carried out in Germany on the basis of EU Regulation (EC) No. 1107/2009 (EC 2009b) and the German Act on plant protection[9]. The Europe-wide approval of an active substance is valid for ten years for the first approval, and 15 years for renewed approval. After this period a new application must be made. This provides an opportunity to examine whether approval is still justified in the light of advances in science and technology. The evaluation and authorisation of the actual plant protection product is carried out in a second step by the relevant Member States. There are currently no specific provisions concerning nanoscale active substances and other nanoscale components, respectively, in plant protection products. However, on behalf of EFSA, RIVM (Dutch National Institute for Public Health and the

[8] EU Chemicals Legislation Finder https://echa.europa.eu/legislation-finder

[9] Gesetz zum Schutz der Kulturpflanzen (Pflanzenschutzgesetz - PflSchG)

Environment) provided a report which compiles and structures information necessary for an environmental risk assessment of nanomaterials to support EFSA in preparing a future guidance for applications of nanoscience and nanotechnology in the food and feed chain (Quik et al. 2020).

The authorisation of **medicinal products for human use** in the EU is regulated by the revised version of the Directives 2001/83/EC (EC 2001a) and their national transpositions, in Germany the Medicinal Products Act[10]. Marketing authorisation procedures exist on an EU wide level (mandatory for new active substances in a centralised procedure), for groups of EU Member States (decentralised procedure and mutual recognition procedure) and as national procedures. Initial approval is for five years, after a renewal, authorisation is usually granted for an indefinite period of time. The decision on granting a marketing authorisation is based on comparing risks and benefits for a medicinal product. The outcome of the environmental assessment, however, is not considered in the risk benefit balance for human medicinal products. The environmental risk assessment is a phased and tiered approach with initially very limited data requirements. Only active ingredients above a certain dosage proceed to a study based assessment. AdMat or nanopharmaceuticals are presently not specifically considered, although it is known that the standard environmental risk assessment approach may not be suitable (Berkner et al. 2015). In 2019, the directive for **veterinary medicinal products** 2001/82 EC (EC 2001b) was replaced by the EU regulation 2019/6 (EU 2018b) of the European Parliament and of the Council, which is applicable as of 2022. Based on both legal provisions, the potential environmental risk posed by a medicinal product is to be assessed and inspected for harmful environmental impacts. The regulation defines novel therapy veterinary medical products which also consider products issued from nanotechnologies. Annex II specifies terms, and technical requirements for presenting quality, safety and efficiency of active substances, for which market authorisation is intended (EU 2021). Beside others, it includes advice how to deal with veterinary medicinal products manufactured using nanotechnology, in particular for use in drug delivery systems.

Food contact materials are regulated according to EC 1935/2004 (EC 2004) stating that they may not release any substances in normal or foreseeable uses, which constitute a health risk to consumers, lead to an unacceptable change in the composition of the food or impair foods in terms of odour, taste, texture or appearance (so called organoleptic properties). This regulation already states that “New types of materials and articles designed to actively maintain or improve the condition of the food (active food contact materials and articles) are not inert by their design, unlike traditional materials and articles intended to come into contact with food. Other types of new materials and articles are designed to monitor the condition of the food (intelligent food contact materials and articles). Both these types of materials and articles may be brought into contact with food. It is therefore necessary, for reasons of clarity and legal certainty, for active and intelligent food contact materials and articles to be included in the scope of this Regulation and the main requirements for their use to be established. Further requirements should be stated in specific measures, to include positive lists of authorised substances and/or materials and articles, which should be adopted as soon as possible.” A specific regulation (EC 450/2009) (EC 2009c) was released later on to clarify information requirements with respect to active and intelligent materials and articles intended to come in contact with food.

3.3 Occupational Safety and Health

Occupational safety and health is regulated on a subsidiary basis in the EU. To protect workers from hazardous substances, there are three directives at European level that set minimum standards for safety and health. These are the Chemical Agents Directive 98/24/EC(1) (CAD), the Carcinogen and Mutagen Directive 2004/37/EC(2) (CMD) and the Asbestos Protection

[10] Gesetz über den Verkehr mit Arzneimitteln (Arzneimittelgesetz - AMG)

Directive 2009/148/EC(3). Those minimum requirements of the EU directives must be transposed into national law by the Member States. Occupational safety and health regulations are directed to the employer, who must take effective measures to protect workers by means of a risk assessment. The chemical agents directive 98/24/EC (EC 1998) defines the terms "chemical agent" and "hazardous chemical agent". The latter includes, in addition to substances and mixtures classified on the basis of hazard properties according to the CLP Regulation, other substances, mixtures and also articles that may pose a risk to the safety and health of workers, e.g., through dusts released during processing. Due to this broad definition, hazardous activities involving materials are always covered by occupational safety and health law, even if they are not placed on the market, are unintentionally produced or are released from waste.

Summary Chapter 3

EU chemicals legislation in general also cover AdMat, however most of them neither explicitly mention AdMat nor provide specific requirements for most AdMat. Some regulations, however, include provisions and/or guidance specifically addressing nanomaterials. Due to their complexity and broad possibilities for application, the distinction of an AdMat being a “substance”, “mixture” or an “article” might be hampered which challenges legal clarity on regulatory requirements.

4 Set criteria for materials of concern and a system to identify them

A systematic approach is needed to identify those materials within the broad landscape of AdMat which pose a concern to human health and the environment from different perspectives. Such an approach needs an institutional backbone which ensures efficient information exchanges of affected stakeholders at an early stage. From the perspective of chemicals regulation and risk assessment, a **National Interagency Working Group was recently established in Germany which aims at developing a foresight and early warning system for AdMat**. It intends to share views and knowledge on AdMat based on early warning signals and to discuss regulatory options, if needed. This approach is currently focusing on the exchange on a national level, however might be used as a blueprint for **establishing similar platforms in other EU Member States, within Europe or on international level (e.g. within OECD)**. In order to allow networking and co-creation of important elements such as early warning systems for AdMat between Member States,**– a regular exchange should be established at EU level** (e.g. in a Round Table format).

4.1 Establish horizon scanning and early warning systems

The German Interagency Working Group firstly deals with foresight and aims to keep pace with innovations **by applying horizon scanning instruments** on a regular basis. Generally speaking, "horizon scanning" describes an assembly of foresight technqiues for "scanning the field" with the aim to detect new developments at very early stages in various sectors to assess possible influences of these developments on the society. More precisely speaking in the context of AdMat, the German Interagency Working Group is interested in new material developments, new material types or new technological changes and their benefits and challenges considering human and environmental risks as well as other aspects like resource consumption, circular economy and climate change. Horizon scanning is often based on desk research but may involve a wide variety of sources, most importantly the internet is used for searches for publications, information from repositories, and conference programs as well as non-scientific sources likes blogs or social media. Equally important is the direct interaction with experts from government and agencies, legislative bodies, non-governmental organisations, international organisations and companies as well as research communities and industry. A solid horizon scan should allow to anticipate "future developments". **The German Interagency Working Group secondly is establishing an early warning system for AdMat** to identify materials that may pose a concern with respect to human or environmental safety. **Generally speaking early warning systems consist of four steps. Early warning signals are picked up in a first screening step** and are then **evaluated and substantiated in the second step**. In a **third step a risk scoring and prioritisation is undertaken** to identify those materials that require a detailled follow-up. **The last step ends with an assessment, if existing legal frameworks already adequately cover these newly identified risks and by identifying and proposing the best option to act.**

4.2 Identify materials of concern in the screening step

Even though AdMat are not intented to be dangerous to human and environment, it is necessary to identify from the variety of all materials those that may give raise for concerns and/or pose challenges for chemical safety or other aspects of sustainability like circular economy. Any potential concern should be taken seriously and clarified at the earliest possible stage of development.

However, this points to a fundamental problem when it comes to adequately mapping the risks of materials to humans and the environment in the context of European chemical safety. A "hazardous substance" or "hazardous mixture" is defined according to Annex I to Regulation (EC) 1272/2008 (EC 2008a). But there is a fundamental difficulty to allocate the term "material" to the terminology in chemical safety regulation. To solve this problem the definition " hazardous chemical agents" in Council Directive 98/24/EC (EC 1998) on the protection of the health and safety of workers from the risks related to chemical agents at work can be used as a starting point. This definition covers beyond substances and mixtures also materials, articles and waste, if "the way it is used or is present in the workplace, present a risk to the safety and health of workers". With a glance on current discussions on "substances or chemicals of concern"[11], this definition can easily be extended to risks for human and environment in general and by criteria for sustainability.

To identify materials that give rise for specific concerns we propose to implement the term "materials of concern" along with criteria to decide whether or not a material falls under that term. These criteria should apply to all materials and are not limited to AdMat only. It is important, especially for communication to the general public, that the concern does not usually correspond to the "very high concern" according to the REACH Regulation and that an initial concern can also be dispelled by valid data.

Proposal for an identification of "Materials of Concern"

A "Material of Concern (MoC)" is

- (i) a material meeting the criteria for classification as a "hazardous substance" or "hazardous mixture" within the meaning of the criteria set out in Annex I to Regulation (EC) 1272/2008, or
- (ii) a material from which hazardous substances or mixtures according to (i) can arise or be released during its production or over its life cycle, or
- (iii) a material which does not meet the criteria (i) or (ii) but which, because of its morphological, physico-chemical, chemical, (eco)toxicological or release properties, could pose a risk to human or environment during its production or over its life cycle, or
- (iv) a material which could pose a concern regarding additional sustainability aspects.

This definition covers under (i) **all materials that are classified as a hazardous substance or mixture due to their intrinsic properties**. Responsible for classification is the person placing the material on the market. It is maintained, on the basis of a notification obligation, in the European Classification and Labelling Inventory[12], and is not harmonised. This means that different classifications may well be listed in the inventory for a given material. Under certain conditions, Member States, manufacturers, importers or downstream users can initiate a harmonised classification, which then applies throughout the entire internal market. One current example is the classification proposal for rigid multi-walled carbon nanotubes initiated by Germany.

Group (ii) covers **materials that are in the legal sense articles or waste and therefore not subject to CLP, but which may release substances or mixtures classified as hazardous during their life cycle**. These are not labelled with hazard symbols, nor a safety data sheet is

[11] "Chemicals of concern" are descripted by ECHA: https://echa.europa.eu/documents/10162/22372335/reach_clp_tips_chemicals_of_concern_en.pdf/ca9abe64-609a-4fcb-9e82-3dfd7c69fdc3; "Substances of concern" are mentioned in European Commission (2020a)

[12] https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/cl-inventory/view-notification-summary

required for industrial users. It can be assumed that a large number of AdMat or products made from them fall into this group, e.g., because they contain substances classified as hazardous in an initially solidly bound form, but which can be released again, at the latest at the end of the life cycle. One example are materials in electronic components, some of which are already subject to restrictions based on the regulations for electronic waste.

Group (iii) then **covers materials that may pose hazards to humans and the environment that are not adequately covered by the current hazard properties of the CLP Regulation**. The classification system for chemical substances and mixtures has been developed over more than 50 years, mainly for industrial chemicals. The focus is therefore on adverse effects for humans and the environment that are directly related to the chemical composition. For materials and thus also for AdMat, however, physical characteristics and morphology are also of high relevance. A well-known example of a morphology related hazard are respirable fibres ("fibre dust"). The example of asbestos shows that the fibre form in combination with a high biopersistence leads to a carcinogenic effect that is difficult to predict with "classical" toxicological test methods. Granular biopersistent particles can also lead to chronic health disorders if they enter the distal lung, accumulate there due to their biopersistence, and over time (especially at high exposure doses) lead to chronic lung inflammation due to impaired lung clearance mechanisms. A whole range of substances have already been classified as hazardous due to these effects. However, substance specific experience in humans or from animal experiments is decisive for this. So far, the CLP Regulation does not provide morphologically based cross-substance classifications (e.g., related to the toxicity of granular biopersistent particles (GBP) or the 3D-fibre principle[13]). Group (iii) also includes environmental hazards that are not adequately covered by the current classification rules. Here, this concerns persistencies, accumulation in environmental organisms, environmental mobility, ecotoxicity to further organisms, and endocrine distrupting properties. Persistence combined with toxicity and accumulation in environmental organisms (PBT) but also high persistency in combination with high bioaccumulation (vPvB) is even treated as a "very high concern" under REACH. This paradigm is currently used, for example, for the restriction of primary microplastics in products.

The proposed definition is intended to make it clear that European chemical safety, which relates to substances and mixtures, only insufficiently covers possible risks of AdMat to humans and the environment, mainly because

- morphological hazard characteristics are not or not sufficiently taken into account by the classification system, and
- in the case of products and waste, information necessary for a risk assessment and definition of measures is not adequately generated and communicated along the supply chains.

For the latter, it has to be kept in mind, that loss of necessary information is highly critical for waste products with unknown building blocks and properties. Additionally, waste and recycling facilities are areas where knowledge on the treated items is generally lower compared to production sides.

The definition should help to identify risks of AdMat as exhaustively as possible as a basis for a targeted governance. **It is recommended to initially use this definition in the context of horizon scanning and in the screening phase of early warning systems. In particular, for the groups (ii) and (iii) of this concept still more detailed criteria have to be established, and specific examples would be helpful as well. The extent to which additional**

[13] In this context, 3D is understood as dimension, dose, durability.

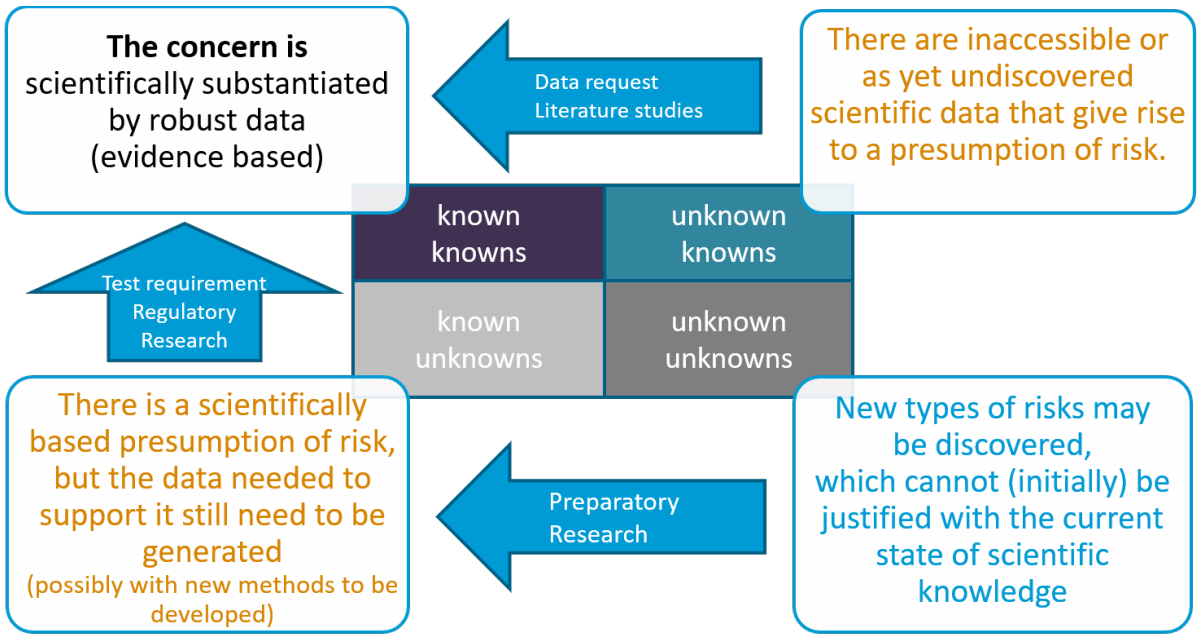
sustainability criteria such as negative impacts on the circular economy, carbon footprint and resource efficiency are taken into account (group iv) should also be examined. It should be noted here, that the German Interagency Working Group on AdMat currently is using the “material of concern” concept and is working on specific criteria.

4.3 Strengthen signals and enhance scientific robustness of the information

While the first phase of an early warning system deals with detecting early warning signals, these signals then have to be strengthened in a second phase, meaning that additional evidence is needed to verify the intial concern. In this context, the scientific robustness of the data basis for a "material of concern" is of central importance (Figure 1). Ideally, evidence-based risk assessment is provided on a reliable data basis. However, this is usually not the reality in the field of innovations. The most common case is that there is only a “justified assumption” of a "material of concern", e.g., from the knowledge of already known materials having a similar structure and/or composition. However, the data required for evidence must still be generated, e.g., via legal testing requirements or in the context of research projects. It may also be that data already exist but has not yet been identified as “relevant” for the specific problem or is not generally “accessible”. In these cases, literature studies and regulatory data requirements can improve and substantiate the scientific evidence.

The most difficult concern, but often the most problematic in terms of public perception, relates to novel risks, particularly in the case of innovations, that cannot be verified by the current state of knowledge or by the current state of the art. Here, at least minimum standards to avoid high exposure and high mindfulness to identify these risks as early as possible should be in place. In addition, well-equipped and continuous risk research accompanying the development and innovation process reduces the probability that new risks to humans and the environment will not be identified until it is too late.

Figure 1: Ways to scientific evidence for risk governance

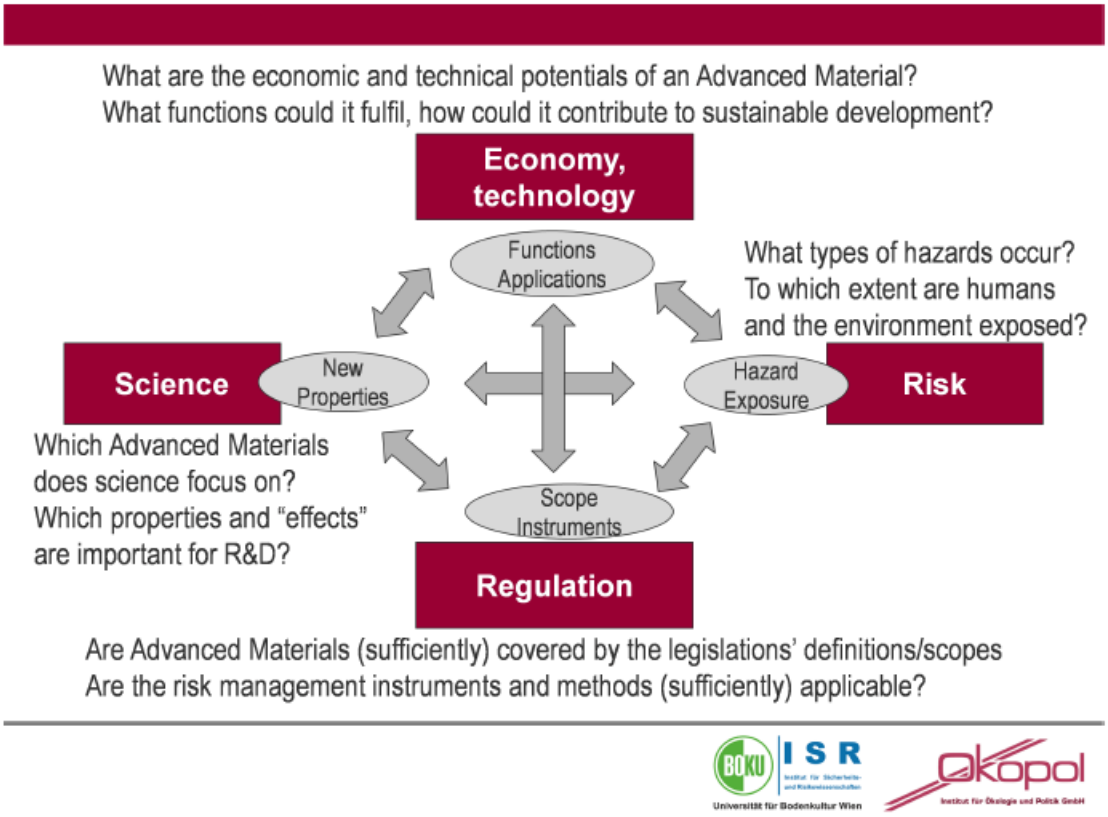


Source: Packroff 2019

One way of approaching AdMat regarding their relevance for action from different perspectives at an early stage was presented in the framework of the departmental research project on

AdMat and their implication for chemical safety (Giese et al. 2020). In this project, relevance criteria for AdMat were developed which aim to identify those AdMat that should be subjected to further assessment and potentially subsequent actions. In the project report, relevance is described in four dimensions, which are interrelated but can be assessed separately (Figure 2). The reason why an AdMat is identified as relevant would then be used to decide where to focus on and what information to collect as the next step. **The relevance criteria used in this approach may also support horizon scanning, while the data needs presented to decide on "relevance" may be also applicable to strategically address signal strengthening.** Furthermore, the combination of various perspectives enables to identify "relevance" in a multidimensional manner to further differentiate between various AdMat. With respect to chemical safety and circular economy of AdMat, the study proposes a first attempt to provide criteria that may facilitate to identify materials that pose a concern to negatively impact human and/or environment.

Figure 2: Four dimensions of relevance developed by Giese et al. 2020



Source: Reihlen 2020

4.4 Carry out risk scoring

Once concerns have been confirmed, either by gathering additional evidence or by verifying the scientific robustness of the data, the next step is an initial risk scoring. Unfortunately, there are only few approaches described for risk scoring that can be directly applied for AdMat. **As a simple, elegant and generic approach, NESSI is proposed, which was developed by BfR.** It should be noted that the **NESSI scoring system** was intentionally created as a more generalised approach to risk scoring such that the system would be applicable for many different hazards and scenarios. Thus, it was not specifically developed for AdMat. **The German Interagency**

Working Group on AdMat will apply NESSI and thereby gradually modify/improve it in future to better meet the needs of AdMat. In its current version, NESSI uses the following criteria:

- **N Novelty** (old versus new). Novelty describes whether a material is entirely new or just has a new application
- **E Exposure** (low versus high). Exposure describes the expected exposure by the AdMat
- **S Severity** (low versus high). Severity describes the expected potential health or environmental effects in case of exposure
- **S Scope** (narrow versus wide). Scope describes the expected number of individuals or ecosystems with significant exposure
- **I Immediacy** (moderate versus urgent). Immediacy describes whether such a scenario is expected in short-term or whether it will only become relevant further down the line

Importantly, when speaking about early warning signals and possible risks of AdMat, one needs to be aware that this is the field of "newly and emerging risks", which broadly speaking differentiates between:

- "Newly created" due to new substances, new technologies etc.
- "Newly identified" due to the fact that new scientific results allow to identify a risk that previously was unkown. In this context also the risk perspection can play a role as the public perception of risks may influence decision making.
- "Increasing risks" due to combined or cumulative effects or due to novel applications.

Often the focus with respect to novel technologies such as AdMat is solely on the identification of possible "newly created risks", which is understandable but nearsighted.

Summary Chapter 4

Strategies have to be developed to identify a potential concern for safety and sustainability at the earliest possible stage of innovation of AdMat. Within such an early warning system, first of all appropriate criteria are needed to derive a concern. Here, the term "materials of concern" is proposed to enable identification on a screening level. These initial concerns have to be supported or refuted by additional scientific data. In case the concern substantiated, the risk has to be described or at least estimated, e.g. by a scoring system as the proposed NESSI system. In Germany, an Interagency Working Group was established to inter alia develop and apply early warning assessments.

5 Be regulatory prepared for emerging technologies

Importantly, at the last step of an early warning system existing legal frameworks are reviewed to verify if they adequately cover the newly identified risks. This review may reveal needs for adaptations of existing legal frameworks. This step is accompanied by identifying and developing recommendations on the best option to act. The overaching aim of this task is to allow regulatory preparedness in view of emerging technologies and associated potential risk. Regulators and policy makers must be capable to anticipate the regulatory challenges posed by emerging technologies, particularly with respect to human and environmental safety challenges. This requires that regulators become aware of and understand innovations sufficiently early to take adequate actions, and that appropriate regulatory tools are modified or newly developed, as needed. Regulatory Preparedness (OECD 2020a) helps to ensure that innovative materials and products undergo suitable (and if appropriate, adapted) safety assessment before entering the market.

5.1 Shape appropriate regulation for advanced materials

For some AdMat it is currently unclear whether or not they are covered appropriately by current legislations on chemical safety. As already mentioned in the previous chapters, a major hurdle is to apply the terms "substance", "mixture" and "article", as defined in European chemicals legislation, to a specific material. Thus, main emphasis with regard to good governance of AdMat should follow the objective to **review relevant legislations and corresponding instruments for risk assessment if they are "fit for purpose"** to ensure reliable and adequate assessment and management of potential risk from the diversity of AdMat**. If such a review reveals that safe handling of (certain types of) AdMat cannot be ensured by existing legislation and corresponding risk assessment instruments, those gaps have to be closed swiftly**. Due to the diversity of AdMat, no general approach can be followed to perform such an analysis as (1) considerations for the different legislations will depend on the materials on the market and their intended application area (see also chapter 3) and (2) consideration on risk assessment will depend on the specific material type. However, as in principle AdMat are covered by existing legislations and as there is no general need for an exclusive risk management of AdMat, a separate regulation specific for AdMat should not be aimed for.

Nevertheless, already now, gaps in existing obligations for downstream users and on articles can be observed which - although not exclusively relevant for AdMat - are further underlined by the complexity of AdMat. While the REACH Regulation provides comprehensive obligations for manufacturers and importers of substances in the context of registration, there are very limited obligations for importers of articles unless they are specifically regulated in a sector-specific legislation such as e.g., cosmetics or food contact materials. **To ensure sufficient information on imports, the same safety requirements should be met, regardless of whether a material on the European market is manufactured within the EU or outside.** Also for downstream users who combine substances to (new) materials without chemical reactions, only limited obligations apply. **Whether such materials are considered as article or as a substance/mixture should not lead to a reduced level of protection. It is therefore necessary to ensure that for such cases sufficient risk assessment data are available as well.**

Another aspect concerns the relation between safe chemicals, circular economy and resource conservation. **For reasons of health, environmental and resource conservation, aspects of circular economy are becoming increasingly important** as mirrored in the Circular Economy Action Plan of the EU (European Commission 2020b). Circulatory aspects must in particular be

taken into account in the context of safe handling AdMat as due to their increasing complexity they may challenge established approaches. **The longevity, reparability, and recyclability of AdMat and their products and applications should be taken into account** during early stage of development as substances of concern and complex materials may negatively affect the recyclability of products.

Furthermore, various surveys and publications identified that for AdMat pharmaceuticals and medical products offer essential fields of application (ECHA 2019; Giese et al. 2020; Oomen 2020)[14]. For these applications especially encapsulated or so called responsive (nano)materials[15] are of interest.

The current pandemic situation caused by Covid-19 has actually promoted the development and use of AdMat for health care, e.g., nanoformulated vaccines, new diagnostic tools, the use of nanomaterials in masks or for desinfection (*inter alia* within Nature Nanotechnology 2020 and Verma et al. 2020, but also[16]). It is expected that similar developments might be applied/used in other sectors as well, such as cosmetics, food or biocides[17]. It also should be noted that so far not in all sector- or product-specific regulations nano-specific provisions have been implemented. In particular, the regulation on plant protection products needs obligations to identify nanoscale active substances and to adequately assess the hazards and risks of these substances and their products for human and environment. Specifications for information requirements are needed to allow an adequate environmental and human risk assessment of nanoformulated biocides and their products. In addition, for plant protection products, biocidal products but also for pharmaceuticals existing regulatory guidelines need to include AdMat and appropriate guidance for environmental and human risk assessment are necessary to be developed.

Clear efforts are required to support the safe handling of AdMat in the mentioned applications. This already applies to simple nanomaterials but is even more relevant for further material developments. Two main corner stones are relevant for the implementation of legal obligations in relation to safety of AdMat. Those are **the availability of agreed methods for obligatory data collection and assessment as well as the availability of appropriate guidance on risk assessment**.

5.2 Develop appropriate assessment methods in a timely manner

To achieve regulatory preparedness, **it is essential that legal requirements keep pace with innovation.** This applies in the first instance to measurement, testing and evaluation methods referred to in the regulation. They are subject to high requirements in terms of informative value, availability, practicability and legal certainty. The successful development and adaptation of methods includes an often long lasting phase of evaluation, interlaboratory tests and standardisation before a method is accepted as sufficiently "ready for regulation". In particular method validation (Figure 3), which needs to demonstrate the relevance and reliability of a method for a specific purpose and its robustness, needs considerable resources. In consequence, availability of accepted methods lags behind material development. However, accepted methods

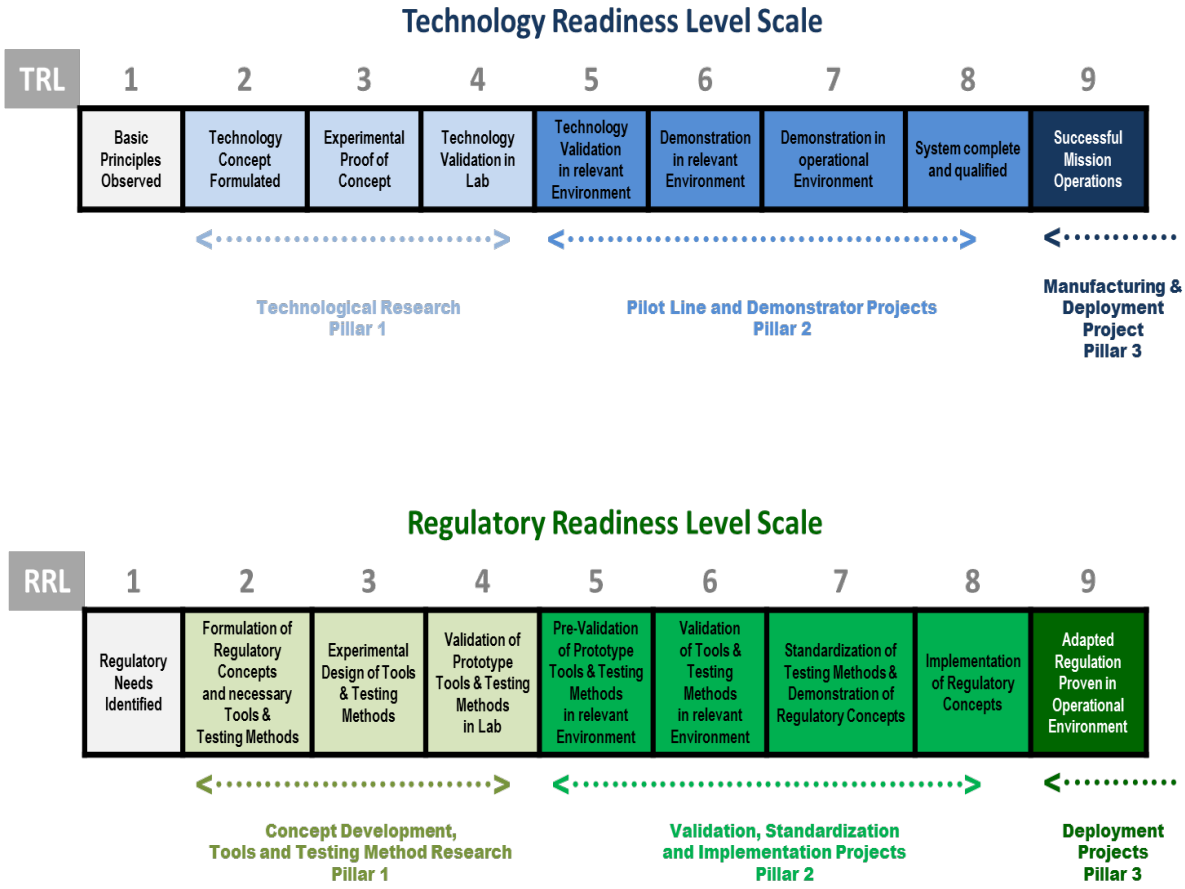
[14] ERA-Net on Nanomedicine https://cordis.europa.eu/project/id/723770
[15] Materials that can reversible change critical properties upon external stimuli in order to activate specific functions.
[16] EU H2020 Project ASINA – „What's new about ASINA's Covid-19 activity", https://www.asina-project.eu/whats-new-about-asinas-covid-19-activity/; Nano the Magazine for small sciences (2021) Pandemic Protection Is Accelerating Investment In Artificial Intelligence And Nanotechnology. https://nano-magazine.com/news/2021/1/2/pandemic-protection-is-accelerating-investment-in-artificial-intelligence-and-nanotechnology; Examples on nanoenabled health care products that have occurred during the Covid-19 pandemic: https://www.azonano.com/news.aspx?newsID=37431, https://www.silvernanofacemasks.com/; https://sonoviatech.com/; https://www.cmddiffusion.com/product-page/product-page; https://anticovidpaper.com/en; https://nanosept-disinfectant.com/hospital-disinfection/hungarian-disinfectant-innovation-in-the-fight-against-coronavirus/
[17] EC Workshop on Safe and Sustainable Smart Nanomaterials (2020) https://ec.europa.eu/jrc/en/event/workshop/ec-workshop-safe-and-sustainable-smart-nanomaterials

are a necessary prerequisite for well enforceable legal regulations for the protection of humans and the environment.

With regard to Regulatory Preparedness it is helpful to make progress and remaining developmental steps transparent. To this end, **we propose a system for mapping the regulatory readiness of measurement, testing and risk evaluation methods and tools.** It was presented by BAuA in 2019 in the High Level Group "Materials" of the EU Directorate General for Research and Development (Figure 3). The description of 9 "Regulatory Readiness Levels (RRL)" is closely following an analogous scale of "Technology Readiness Levels (TRL)" and comprises the phases of development or adaptation, validation, standardisation and implementation as well as introduction and evaluation in practical application. The ideal case is a coordinated procedure with regard to both scales with the aim of having standardised measurement, testing and evaluation methods and an adapted regulation (RRL 8) already available for the market launch of an innovation (TRL 8). The RRL scale helps regulation and research funding institutions to visualise research, development, and policy needs and progress in order to continuously adapt existing legislation and regulations as well as assessment strategies. **To keep pace with innovation, RRL should be at the same level as the corresponding Technology Readiness Level (TRL) of relevant AdMat.**

A continuous development of required test methods should be guaranteed. This can be enabled by the allocation of appropriate funding (amount, timeframe). The European Commission should ensure timely development of necessary test methods. Therefore, **it is recommended to strenghten the efforts at European Institutions (e.g., JRC and ECHA) to support test method development detached from ISO/CEN standardisation activities and from the development of non-animal testing methods for safety assessment**.

Figure 3: Comparison of Technology Readiness Level Scale to Regulatory Readiness Level Scale



Source: Packroff 2019 (Technology Readiness Level Scale taken from: European Commission, High-Level Expert Group on Key Enabling Technologies (2011), Final Report)

Summary Chapter 5

Regulators and policy makers must be capable to anticipate the regulatory challenges posed by emerging technologies, particularly with respect to challenges for human and environmental safety. Main emphasis should follow the objective to review relevant legislations and corresponding risk assessment instruments if they are “fit for purpose”. If such a review reveals that safe handling of (certain types) of AdMat cannot be ensured by exisitng legislation and corresponding risk assessment instruments, those gaps have to be closed swiftly. Two main corner stones are relevant for the implementation of legal obligations in relation to safety of AdMat. Those are the timely availability of harmonised methods for obligatory data collection and assessment as well as of appropriate guidance on hazard, exposure and risk assessment.

6 Promote Safe and Sustainable by Design

With regard to the Chemicals Strategy for Sustainability of the European Commission (European Commission 2020a) "Overall sustainability [of chemicals] should be ensured by minimising the environmental footprint of chemicals in particular on climate change, resource use, ecosystems and biodiversity from a lifecycle perspective." Due to their potentially broad application areas and their complexity, sustainability is of particular importance for material innovations. Potential chemical risks and accompanying environmental footprint of these materials and their applications need to be understood and should be managed over the entire life cycle at an early stage to achieve a positive contribution to the European Green Deal and the Chemicals Strategy for Sustainability, but also to the UN Sustainable Development Goals (SDG) of the Agenda 2030.

The aim to minimise the use of resources, risk, pollution and waste during the whole life cycle of chemicals is not a new one. This is the central idea of the sustainable chemistry concepts[18] (including green chemistry). The principles of sustainable development (German Federal Government 2018) include a consequent utilisation of sustainable development as guiding principle for all areas/ decisions, to take global responsibility, a preservation of our natural resources, strengthening sustainable management, preservation and improvement of social cohesion in a open society as well as to use education, science and innovation as driver for sustainable development. Additionally, in the past years several initiatives worldwide have been engaged in the development of various models and tools for Safe(r) by Design (SbD) in particular for nanomaterials with main focus on human health and workplace safety, respectively (OECD 2020a).

The so-called Safe(r)-and-Sustainable-by-Design (S&SbD) concept could be understood as an extension of the SbD concept developed in the course of nanomaterial safety research due to the inclusion of further considerations regarding sustainability beyond chemical and material safety. **S&SbD should be understood as a pre-market approach that guides producers through their innovation and development process of materials and products.** The utilisation of the concept already in the innovation and development phase has the advantage that these stages provide the greatest scope for action for safe and sustainable innovations. In addition, as European chemical safety regulations oblige manufacturers and importers to carry out a systematic assessment of hazardous properties when a product is or should be placed on the market (i.e., specific product groups, classification and labelling according to the CLP Regulation) or after a specified annual production volume has been exceeded (registration according to the REACH Regulation), S&SbD can help the producers to identify gaps in product safety and prevent possible regulatory challenges in time.

Depending on its design, this approach can support to identify and minimise the potential health and environmental risk of a material innovation. It can help to recognise wether or not the overall (or specific aspects of) sustainability of a material innovation is supported as well as to inprove its sustainability if needed.

The task of authorities and decision makers in that context is to establish a framework under which the terms "safety" and "sustainability" can be agreed on with regard to material innovation, chemical safety and sustainable chemistry, to provide incentives for S&SbD developments as well as to support knowledge generation and transfer.

[18] OECD Sustainable Chemistry: https://www.oecd.org/env/ehs/risk-management/29361016.pdf; ISC3- International Sustainable Chemistry Collaborative Centre: https://www.isc3.org/en/about-isc3/sustainable-chemistry.html

To promote S&SbD and to avoid doubling of efforts, existing results, knowledge, and principles of sustainable chemistry should be integrated into the future work on S&SbD, and initiatives of both concepts should be continued hand in hand.

6.1 Develop criteria for safe(r) and sustainable by design (S&SbD)

Indeed, AdMat have the potential to provide alternatives that are able to substitute hazardous or less sustainable materials, chemicals, products or processes. However, care should be taken to not develop regrettable substitutes. For a successful realisation and acceptance of S&SbD approaches and their application for AdMat agreed criteria and indicators for both safe(r) by design and sustainable by design are key elements. **Criteria and indicators for selecting sustainable chemicals were proposed by UBA's Guide on Sustainable Chemistry** including *inter alia* criteria and indicators for chemical safety, resource consumption in the value chain, emission of greenhouse gases in the value chain and during use, and emission potential during the use phase or responsibility in the value chain (Reihlen et al. 2016). **As for AdMat the whole life cycle is of particular importance, these criteria should be reviewed and complemented by criteria to address particularities of materials** (e.g., risk pattern of particulate substances) taking into account also the proposed considerations on materials of concern (see chapter 4) as well as to cover further life cycle stages, and criteria for social (e.g., social working conditions), and economic aspects of sustainability (e.g., successful and long-term economic activities within planetary natural capacity). For the establishement of S&SbD approaches for AdMat, their influence on the reduction of resource uses, the promotion of re-use and recycling but also the extent of energy consumption, possible rebound effects[19] or burden shifting are of particular relevance beside chemical safety. Nevertheless, chemical safety is one corner stone within S&SbD and should not be offset by criteria for sustainable by design, because an AdMa or its application will not achieve overall sustainability if it can cause chemical risk for human or the environment.

To make S&SbD a success, cooperation and networking on national, EU and international level is needed. This includes contribution from industry, academia, civil society and authorities to find common understanding on the meaning of S&SbD, to discuss and agree on corresponding criteria and indicators as well as to foster knowledge transfer to step towards S&SbD material innovations.

Within the current European Research Framework Horizon 2020, **projects like SUNSHINE, HARMLESS and DIAGONAL** are funded which aim to develop criteria, strategies and guidance for S&SbD of AdMat[20]. These initatives **should be engaged into the dialogue when establishing agreed criteria and approaches for S&SbD for AdMat whereby the development of these criteria should be coordinated with the development of general S&SbD criteria within in the framework of the Chemical Strategy for Sustainability of the European Commission[21]**. For the aim of deducing criteria for sustainable design of chemicals, materials and products, the European Commission recently published a mapping study which identifies relevant policies and initiatives implementing sustainability criteria and lists associated R&I efforts (European Commission 2021). In the context of these initiatives **it should be kept in view, that design considerations may also be applied at the level of entire systems**, e.g., a reduced burden due to decreased demand of materials achieved by e.g.,

[19] In policy analysis, the rebound effect denotes secondary effects of a technological or political measure that run contrary to the original intent of the primary measure. Rebound effects are triggered by a development or measure and reduce the associated and usually intended effect (De Haan et al. 2015)

[20] NMBP-16 projects: https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/nmbp-16-2020

[21] First reflections on how to consider sustainability aspects within REACH are presented in Führ et al. 2019 and Bunke et al. 2020

chemical-free alternatives, alternative business models, sustainable consumption, and change of behaviour.

In addition, **to be able to gather reliable knowledge and to decide at an early stage of material innovation if potential criteria (e.g., on safety) are met, agreed screening methods need to be developed and applied that are scientifically reliable**, e.g., with regard to later requirements of chemicals regulation.

6.2 Empower stakeholders by knowledge transfer and education

It can be assumed that the development of hazardous or unsustainable materials mainly results from unawareness rather than wilfulness. Therefore, **awareness raising and a change of mindset in relation to safety and sustainability of material innovations is an important corner stone as well as empowering developers and manufacturers to identify the impact of their materials on safety and sustainability**. This can be achieved on the one hand when S&SbD approaches are anchored in the vocational and tertiary education system (chemistry, engineering, material research, design, other) by e.g., dedicated professorships, sommer schools, and lectures within graduate colleges. On the other hand, knowledge transfer to companies like SME is needed. This can be realised e.g., by training offers, webinars and guidance. **Education and knowledge transfer should include existing knowledge on hazardous substances and materials as well as sustainability issues, methods and instruments to assess risk and sustainability, relevant regulations as well as information, tools and skills how to step towards safe and sustainable developments**. The master program in sustainable chemistry of the ISC_3 provides an example for the development and implementation of an international study program[22]. Beside activities on education, the ISC_3 is also active in providing platforms for dialogue and knowledge transfer connecting science, entrepreneurs, and industry with the public sector and civil society. In addition, the Substitution Support Portal of BAuA - SUBSPORTplus - already recommends a number of substitution solutions, provides information on existing regulation and available guidance, and is updated on a regular basis[23]. Further possibility for for knowledge transfer and awareness raising on safety and sustainability of material innovations for industry could be the platform on „Advanced Technologies for Industry"[24] of the European Commission which is currently set up to promote the implementation of policies and initiatives with regard to industrial policy approach of the EU. In addition, an approach was developed by the Oeko-Institute that should support developer and producer of nanotechnological products and applications to carry out a preliminary self-evaluation of their own business and activities as a first step. The so-called Nano-Sustainability Check should provide an instrument offering a systematic grid for an integrated approach relative to sustainability aspects of nanotechnological applications (Möller et al. 2012; Möller and Schoßig 2011).

Finally, it is important to be conscious about the fact that S&SbD for AdMat and their applications can lead to conflicts of targets, e.g. due to the inavoidable use a hazardous AdMat for new technology of high social benefit (e.g. revewable engery production) at least in the near and mid-term future. **An interplay of S&SbD together with an Early Warning System** (see chapter 4) **and Regulatory Preparedness** (see chapter 5) **can help to recognise such conflicts in an early stage but also to identify and fill data gaps on chemcial safety and**

[22] ISC3 activities on education: https://www.isc3.org/en/activities/education.html
[23] BAuA Substitution Support Portal: https://www.subsportplus.eu/subsportplus/EN/Home/Home_node.html
[24] Advanced Technologies for Industry platform: https://ati.ec.europa.eu/

sustainability. Furthermore, such an interplay will **support an interdisciplinary discussion on how to decide on or identify measures to alleviate these conflicts.**

Summary Chapter 6

S&SbD should be understood as an approach that supports manufacturers to promote safety and sustainability considerations within their innovation processes of materials, products and their applications. For successful implementation, acceptance and application of S&SbD approaches for AdMat, widely accepted criteria and indicators for both Safe(r) by Design and Sustainable-by-Design are essential. In addition to reducing material risks, S&SbD concepts should also aim at reducing the demand for raw materials, strengthening reuse and recycling, but also consider energy demand, possible rebound effects, and burden shifting. For the idea of S&SbD to be a success, cooperation and networking at national, EU and international levels are necessary.

7 Involve relevant stakeholders and establish mechanisms for interactions

Dialogue is important for an exchange of the diverse perspectives of different stakeholders, to gain insight and understanding, learn about different needs and concerns as well as to harmonise the use of specific terms.

As outlined in table 2 below the interaction between stakeholders can be characterised by three important elements, scientific expertise, trust and rules. Concerning the expertise from science, industry and regulation, it is important to identify the relevant actors such that the interaction will ensure an exchange of relevant knowledge and data, leading to an increased understanding of the subject. The other two elements are closely linked to each other and more difficult to address. Trust between all stakeholders is an important prerequisite for a comprehensive exchange of scientific knowledge and the derivation of recommendations for risk governance. For this to happen, as communication research on the governance of risks posed by nanomaterials has shown, a certain set of conditions must be met, as listed in table 2 below (Reichow 2015). The positive experiences from the dialogue processes on nanomaterials in Germany have also been incorporated into this study.

Table 2: Theoretical framework for an effective governance of nanomaterials in collaborative networks

Level	Analytical Category	Conditions
Actor level	**Substantive learning** Characteristic: *Scientific expertise*	1. Relevant actors collaborate 2. Exchange of knowledge and (risk) data 3. Increased understanding of how to deal with core problems related to nanomaterials risk assessment, and 4. Generation of novel scientific facts
Game level	**Strategic learning** Characteristic: *Trust*	1. Meetings over a longer period of time 2. Intensified actor relations 3. Reliance among collaborators 4. Realization of common goals 5. Disagreement among collaborators is addressed and solved, and 6. Development of additional collaborative activities
Network level	**Institutional learning** Characteristic: *Rules*	1. Development of informal agreements 2. Design of soft rules of behaviour, and 3. Soft rules become “hardened”

Source: Reichow 2015

Depending on the role of the dialogue in an overall process, the aim is to achieve transparency about pros and cons of a certain topic, become aware of it or the multiple social, ecological and/or economical concerns and expectations of the different stakeholders, achieve agreements between different stakeholders or find decisions. Ideally, dialogue also facilitates the mutual trust into the role and position of the other parties.

It is not self-evident that a stakeholder exchange is successful. Stakeholders need to have an interest in an (open) dialogue. This might be hampered by lack of trust, various cultures, ways of communication, or the protection of intellectual property. Transparency and dialogue do not mean that a common understanding or agreement on a subject will be or have to be reached in any case. Also, a subject can become more complex due to various conflicts of goals. Furthermore, it could be the case that not all relevant stakeholders are involved and that important issues may be overlooked.

In general, with respect to efficient stakeholder interactions, recent experiences in the field of nanosafety should be used as a basis for the dialogue on benefits and challenges of AdMat. Therefore, in a first step, established infrastructure (e.g., working groups, councils and dialogue platforms) should be extended to also cover AdMat to pave the way for how to establish and ensure stakeholder interactions in the field of AdMat. As decribed in the following this has happened already for several dialogue platforms.

Within the **research community** there are several well established connections that are currently progressing from the field of nanosafety research towards AdMat. On the European level the EU NanoSafety Cluster[25] is an environment to exchange across the different projects funded under Horizon 2020 and now Horizon Europe. Within Germany, the DaNa cluster[26] follows a similar strategy to link the different national projects funded by the Federal Ministry of Education and Research (BMBF) within the NanoCare and NanoNature frameworks. Both clusters have already expanded their interests beyond nanomaterials and are now more broadly addressing safety research on advanced materials (including nanomaterials). Importantly, these projects are not limited to research but also provide a means for different stakeholders (academia, industry and regulators) to interact. It should be noted, that comparable to nanosafety research, the research community for AdMat needs to be of broad interdisciplinarity bringing together material experts, toxicologists, biologists, modellers and many more.

Applied safety research is certainly one important pillar to address potential risks of innovative materials. However, the current funding mechanisms often do not sufficiently cover aspects related to **standardisation**. In this context, linkages to OECD and ISO are the most important ones to mention. Within the OECD Working Party on Manufactured Nanomaterials (WPMN) an Steering group for Advanced Materials was established in 2021 with the task to provide a proposal how WPMN can address the topic AdMat within the scope of the Working Party and in cooperation with other OECD Working Parties (e.g., Working Party on Biotechnology, Nanotechnology and Converging Technologies). Similarly, ISO has recently initiated a working group on AdMat. Standardisation will be important to clarify aspects of terminology and to support method validation. VAMAS, the Versailles Project on Advanced Materials and Standards, is an international collaborative organisation which was set up to promote the underpinning research and development that is required to be undertaken as a precursor to the preparation of new standards relevant to AdMats. It is intended to facilitate agreed international collaboration standards that will aid trade world-wide. The scope of VAMAS includes materials specification, databases, test methods and design procedures[27].

With respect to **industry stakeholders,** it firstly has to be emphasized that the field of AdMat is very broad and is thus involving many different industry sectors. There are several platforms linking the industry community in the field of AdMat and Advanced Engineering such as the

[25] https://www.nanosafetycluster.eu/
[26] https://www.nanopartikel.info/projekte/cluster-meeting
[27] http://www.vamas.org/

European Technology Platform for Advanced Engineering Materials and Technologies[28] and the Chemical and AdMat Industry Community of the World Economic Forum[29].

Importantly, industry stakeholders include large industries but also small and medium enterprises. Also, it has to be noted that industrial production processes are highly specialised with some companies providing materials only, while others provide products specific parts and pieces that are then assembled by additional industrial players into the final product such that within one production chain many different companies and sectors might be involved.

Regulatory stakeholders are often organised according to the different sectors being regulated by the different European frameworks for chemical safety. Therefore, chemical safety (that broadly speaking would include material safety) is organised on the European level by ECHA but also other European Institutions such as EFSA, both are typically working closely together with national authorities in the different Member States. In the field of nanosafety, different expert panels and working groups have already been established such as the ECHA Nanomaterial Expert Group (NMEG) or the EFSA Working Group on nanoscience and nanotechnology in food/feed. On the European level, according to our knowledge, there is currently no dedicated expert group or working group on AdMat. Within Germany, several German regulatory agencies recently established a **National German Interagency Working Group** that is currently focusing on establishing a foresight and an early warning system for AdMat. This working group will allow to discuss early warning signals and possible regulatory options by considering different perspectives from the beginning. The **Working Group of the Federal Ministries** established for regulatory support of nanotechnologies under the leadership of the Federal Ministry of Education and Research will also be continued under the expanded focus of AdMat.

The annual **International Nano-Authorities Dialogue** of Austria, Luxembourg, Liechtenstein, Switzerland, and Germany discusses current topics in the field of nanomaterials and nanotechnologies related to environmental, health and occupational safety between authorities and representatives from industry, science and NGOs since 2006[30]. At its 14th meeting in October 2020 the Dialogue also included AdMat into its agenda and roadmap.

Furthermore, under the lead of the Dutch Ministry of Infrastructure and Water Management the **Safe-by-Design Policy International Network** (SPINE) was formend. SPINE is an informal network for European policy makers that seeks to share knowledge and exchange expertise, develop and implement the Safe-by-Design concept in new and emerging technologies, and to establish a safe and sustainable economy. SPINE is a consultative body for the promotion and support of low risk technological developments and materials.

Public engagement is also crucial, especially in contexts characterised by high scientific uncertainty and potential for social mobilisation, such as novel materials (Renn 2020). The field of nanosafety offers examples for a variety of public engagement mechanisms that can be applied, reaching from unidirectional surveys to more dialogue oriented deliberative methods, such as the consensus conference on nanotechnology (Zimmer et al. 2009).

It should also be noted that Germany has a long tradition with respect to the **"Nano-Dialogue"**, being established by the BMU and which is now continued in the form of "Expert Dialogues", each addressing a specific topic. The aim of this long-term, continuous exchange with the various

[28] https://www.eumat.eu/en
[29] https://www.weforum.org/communities/chemistry-and-advanced-materials
[30] International Nano-Authorities Dialogue: https://www.bmu.de/en/topics/health-chemicals/nanotechnology/international-nano-authorities-dialogue

stakeholders is to provide socio-political support for scientific and technological developments in the field of nanotechnologies. The last one held in 2019 was focused on AdMat[31].

Summary Chapter 7

Safe and sustainable innovation of AdMat requires a trustful, transparent and open dialogue that allows to gain insight and understanding of the different perspectives, and to learn about different needs and concerns. In the context of AdMat, the dialogue can build upon experience from the established dialogue infrastructure on chemical safety of nanomaterials.

[31] https://www.bmu.de/en/download/5th-dialogue-phase-expert-dialogue-4-opportunities-and-risks-of-advanced-materials

8 Research

Research plays a multilayered role for good governance of AdMat. In the sense of preparatory research, it can help to identify risks to humans and the environment at an early stage and to generate reliable data for this purpose, which at least enables preliminary governance on the basis of the precautionary principle. This also includes the development of new methods and tools for early risk identification and assessment according to the Regulatory Readiness Levels RRL 1 – 4 (Figure 3).

Another area that has often been undervalued in the past is regulatory research, which involves the systematic generation of evidence for specific regulatory measures as well as the validation and standardisation of methods according to the Regulatory Readiness Levels RRL 5 – 7 (Figure 3). However, this also includes research projects which focus on the systematic evaluation of the effectiveness of measures taken (RRL 9).

8.1 Enhance preparatory research to allow safety to keep pace with innovation

The task of preparatory reseach in the context of chemical safety is to identify challenges and pitfalls for human and environmental safety at an early stage as well as to assess their relevance and to propose solutions. It includes exploring new subject areas of relevance as well as to promote research in existing subject areas such as the development of tools, instruments and approaches to address existing areas of activity (see Figure 1). Preparatory reseach is of special relevance for governmental research to be able to encounter new challenges for health and environmental policy in an adequate and timely manner. With regard to AdMat, preparatory research is needed to **provide relevant data which can be used to deduce regulatory needs for action specific for AdMat**. It should also aim to **initiate research to identify adequate alternative testing and assessment strategies to support risk assessment of the variety of AdMat** which may be pushed for standardisation in order to be applied in regulation later on. This research should also **develop and evaluate principles and options that ensure the safe and sustainable development of AdMat** (e.g., alonside the various stages of innovation).

Data collection for basic understanding of the diversity of AdMat and their potential impact on human health and the environment poses specific challenges. While data might be available on the building blocks of many AdMat (if consisting of such blocks), an understanding of their detailed composition and characterisation of their combined properties might be not available, at least for regulators. In addition to that, specific data on hazards to human and environment will be missing for many AdMat in case these cannot be deduced from their building blocks. The same is true for data on behaviour and fate of these materials in the respective biological and environmental compartments. Furthermore, knowledge on the potential of AdMat (or their building blocks) to be released from products and subsequently expose human and the environment or other implications on environmental footprint over the different stages of the life cycle is largely missing. **Preparatory research on potential implications of AdMat and their applications over their whole life cycle should become an integral part of funding of material innovation to ensure safe and sustainable development.**

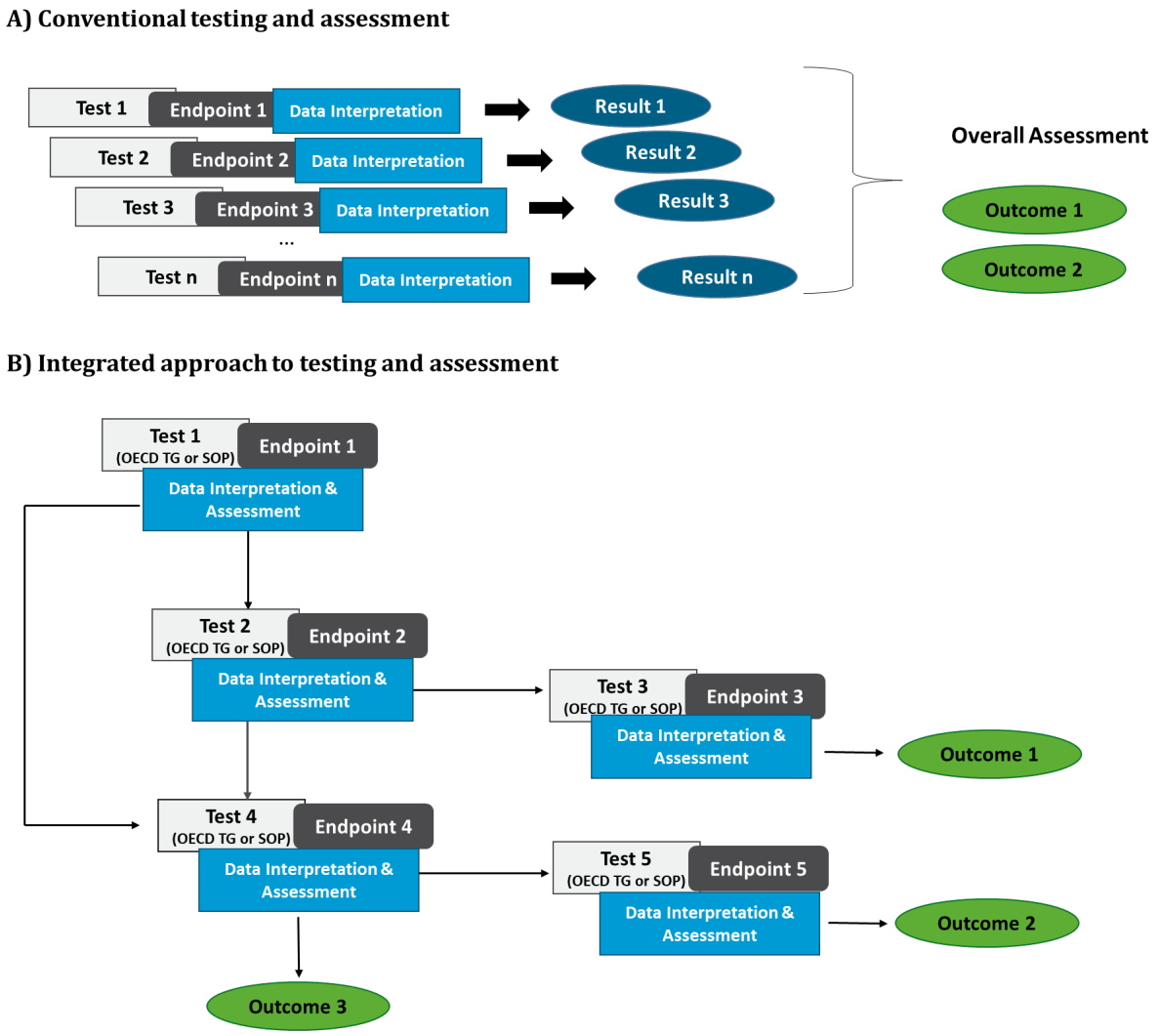
Research needs on alternative methods

In view of chemical safety and the variety of AdMat and their potential applications, no general assumptions can be made regarding their hazard potential towards humans and the environment, their ability to release critical substances from articles, their mobility in the environmental or their potential for (bio)persistency. As of now, no generic or across-substance

approaches exist on how to reliably derive hazard and fate data for AdMat from building blocks of known toxicity, precursors or materials of similar composition. Thus, assessment is currently limited to case-by-case data collection and analysis. Therefore, **preparatory research needs to focus on approaches that specifically allow testing and assessment of AdMat. However, novel approaches should be considered from the beginning.** For instance, **Integrated Approaches of Testing and Assessment (IATA)** offer interesting possibilities to reduce the amount of testing to a necessary minimum. In principle, IATAs offer a logical strategy to integrate exisiting data with new experimental tests and other information such as in silico extrapolations or modelling results and are therefore much more efficient and targeted, compared to conventional approaches (Figure 4).

Figure 4: Integrated Approaches for Testing and Assessment (IATA)

Following a conventional approach, each substance is assessed by considering the outcome of a number of tests that are all conducted and evaluated separately (A) while an integrated approach on testing and assessment (IATA, B) describes a logical combination of tests where the outcome of a specific test determines the next step such that the overall assessments can be conducted with a minimum of new experiments.



Source: own illustration based on the concepts described in Rovida et al. 2015 and OECD 2020b.

Development of IATAs specific for (types of) AdMat would allow to circumvent individual testing and assessment and thus, reduce the efforts and expenses involved. Even though the development of IATAs for chemicals and materials is still in its infancy, there are some research efforts which may also serve as starting point to establish IATAs for selected AdMat[32]. In developing IATAs, **adverse outcome pathway (AOP) concepts** can be helpful. In short, AOPs are analytical constructs that combine existing knowledge to link molecular initiating events triggered by a specific substance via specific and defined key events to a clearly described adverse outcome[33]. The knowledge about such key events supports designing relevant test strategies that in future may even replace complex animal studies. However, as with IATAs, AOPs specific for AdMat are currently not available and need a certain degree of knowledge regarding the molecular/subcellular processes leading to adverse effects.

In addition, **grouping approaches**, as currently under development for nanomaterials, also would greatly support hazard assessment of (types of) AdMat (Giusti et al. 2019; Stone et al. 2020). However, to establish valid grouping hypotheses, scientific effort to identify the key properties which determine a similar behaviour or effect of AdMat or their buidling blocks within a group is necessary. **Nevertheless, in order to deal with the complexity of material innovation, dedicated research funding is needed to develop IATAs, AOPs and grouping concepts for AdMat as those concepts can enable safety assessments with a necessary minimum of resources**.

Research needs on S&SbD

Various research initiatives within EU Horizon Europe are underway focusing on particular aspects of sustainability for AdMat applications e.g., to substitute hazardous materials (i.e., hazardous nanomaterials) by less hazardous ones, on selected life phases or goals of protection (i.e. mainly production phase and worker safety). Further calls for product development near to market launch are intended by the European Commission.

Although it is highly appreciated that safety aspects of material innovations come to the fore of the funding institutions other aspects of sustainability have been hardly covered yet within these initiatives. In that respect, models and tools need to be strengthened by including approaches for consumer and environmental safety and further aspects of ecological footprint. **These considerations need to be integral parts of the general research and development funding of material innovation with sufficient funding for these tasks** instead of being dealt within separate calls. Finally, service oriented business models like chemical leasing should be investigated for their utilisation in material innovations.

In order to ensure safe and sustainable innovation of materials, criteria to assess the safety and sustainability of AdMat are urgently needed (see Chapter 6). These criteria need to be measurable, either qualitatively or quantitatively. Even though it is expected that for many of the classical safety criteria methods will be available, some research effort will be needed to ensure that these methods are also applicable for determining safety of material innovation. However, **future preparatory research needs to focus on the development of concrete criteria to verify sustainability of AdMat** while taking into account existing criteria on e.g., sustainable chemistry or LCA.

Research needs to enhance circular economy of AdMat and their applications

The increased complexity of material innovations and new possibilities to use materials by advanced manufacturing processes give cause of concern regarding (unknown) hazards,

[32] e.g. as developed currently in EU H2020 Gracious for nanomaterials
[33] OECD on AOPs: https://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm

implications for and disturbances of established recycling cycles and thus, raises questions of operators of recycling plants. **Preparatory research should also approach the implications of AdMat for the objectives of a circular economy**. Research is strongly needed to identify AdMat and their applications which will interfere with established recycling processes and to provide solutions for product specific treatment and processing of those applications. Therefore, specialised waste treatment facilities, new concepts of collection and communication and sustainable business cases for waste treatment companies are needed, e.g., in case for high strength or heat resistance AdMat. Innovative waste treatment as well as extended producer responsibility is needed which (e.g., in the case of fibre reinforced plastics) needs to include a separate collection and processing. **Research in cooperation with producers as well as waste treatment plant operators will help to develop approaches which ensure high recyclability of products and the best recycling option for the AdMat in question. Protocols for proper separation** from these applications **and procedures for appropriate recovery and recycling have to be developed.** Proposals for measures should be developed to ensure a safe handling of potentially harmful materials for human and environment during the different steps of recovery. Furthermore, **research investments on economically, socially and ecologically meaningful application possibilities of recycled materials** should be considered.

AdMat in Horizon Europe

The EU Research Programme 2021-26 "Horizon Europe" provides a good framework adressing safety and sustainability of AdMat in parallel to material research and innovation. For the first time, the focus of research is no longer purely on technology support, but there is an orientation towards how to solve global challenges and how to contribute to the UN sustainability goals.

A central element is an European Partnership on Assessment of Risk of Chemicals (PARC). As an initiative of Member State authorities to improve current EU regulatory risk assessment it *inter alia* will deal with challenges which are also relevant for AdMat, i.e. development of S&SbD concepts, innovative and alternative methods, testing and assessment strategies, early warning signals as well as the development of guidelines for the findability, accessibility, compatibility and reusability of data necessary for risk assessment ("FAIR data"). It is supposed that PARC will lead to significant and at the same time EU wide acceptable progress in the areas mentioned which will be also of benefit for pre-regulatory and regulatory measures for AdMat.

However, PARC's focus will be primarily on industrial chemicals. Safe and sustainable AdMat are addressed in the Horizon Europe Cluster "Digital, Industry and Space". Together with the political goal of the European Green Deal and the associated Chemicals Strategy for Sustainability, the development of criteria for S&SbD in a timely manner is an integral part to make that funding programme to a success. The greatest challenge here is to ensure interdisciplinary cooperation between risk and material research as a necessary prerequisite for the success of these funding lines. Also, existing experiences and knowledge from the sustainable chemistry community should be taken into consideration. This certainly requires institutional support. Innovation hubs offer a solution within the framework of Horizon Europe. Several Horizon 2020 projects are currently discussing approaches for a Risk Governance Council for Nanomaterials[34], including in the form of a permanent EU-funded advisory body for research institutions and companies developing nanomaterials. **We suggest to broaden the focus of a future Nano Risk Governance Council to safe and sustainable materials. This should comprise to:**

[34] https://www.gov4nano.eu/; https://riskgone.wp.nilu.no/; https://nanorigo.eu

- identify and make available evidence-based knowledge on principles for S&SbD of AdMat,
- organise a knowledge transfer from risk research to material science and development, in particular for SMEs and support education,
- initiate transdisciplinary research involving relevant actors, and
- support project consortia under Horizon Europe with regard to the UN sustainability goals and the Green Deal.

8.2 Strengthen regulatory research to support good governance with scientific evidence

Verify risk assumptions for legal purposes

To be able to pursue risk assumptions at an early stage is of special relevance for risk assessors, especially in cases if verification of these risk assumptions is not captured by regulatory information requirements. Therefore, **broad research possibilities and scientific freedom with sufficient funding is needed to allow the investigation of materials which are suspected to be of safety concern or pose a regulatory gap**. Adressees for results of this kind of research on AdMat are mainly regulators, however it is also of interest for innovators to avoid investments into material developments which won`t receive market allowance due to safety concerns, inacceptable risks or legal uncertainty.

Develop standardised measurement, testing and evaluation methods

As mentioned above, to make regulation enforceable, agreed harmonised and standardised methods are needed. According to European Law it is the duty of European Commission that those methods are available. While there are a number of initiatives ongoing to develop standard test methods for nanomaterials, it is currently unknown to what extent these methods will be also applicable for AdMat. **A systematic analysis is recommended to analyse if and for which types of AdMat nano-releated test methods could apply and what kind of additions may be needed to also account for the increased complexity of AdMat.** The demand for specific standard tests for AdMat will surely go beyond the need for test methods for nanomaterials as current test method development does not necessarily consider testing requirements of other or even more complex constructed materials, their characteristics, behaviour and effects.

With regard to the Regulatory Readiness Level Scale shown in Figure 3, current research funding focuses primarily on the "laboratory development" of test, measurement and evaluation methods in the sense of RRL 1 – 4 in general. By contrast, the next steps of validation and standardisation (RRL 5 - 7), which are central from a regulatory point of view, are very often not in focus of funding institutions and actors in research. Since Horizon Europe is now focusing more on market-ready innovations (TRL 5 - 8) in the area of technology funding, **the development of agreed testing, measurement and evaluation methods that are ready for regulation should be supported in a adequate manner.** The "Malta Initiative"[35] initiated for nanomaterials offers a good model that can also be applied to other advanced materials.

Evaluate the effectiveness of governance strategies

There is a need for **research activities that evaluate** (in the sense of RRL 9, see Figure 3) **regulations already in place with regard to their practical implementation and effectiveness, e.g., with field studies on exposure reduction**. In principle, effective regulation

[35]Malta Initiative: https://www.bmu.de/en/topics/health-chemical-safety-nanotechnology/nanotechnology/the-malta-initiative/

must be able to reduce human and environmental exposure to hazardous substances to such an extent that the remaining risks are below a generally accepted limit. However, conflicts of objectives might also justify higher tolerance thresholds, if this is supported by society. Apart from the basic effectiveness (performance), the successful implementation of the regulations in practice (compliance) is also of decisive importance. This is particularly necessary for "soft" regulations in order to initiate a timely "hardening". But also for "hard" regulations, which clearly interfere with the free movement of goods and products in the European internal market, evaluation research is advisable in order to learn for future regulation processes. This is an important task and challenge for the higher federal authorities involved and other corresponding EU and Member State research institutions.

Summary Chapter 8

Research plays a multifaceted role for a good governance of AdMat, as data generated under existing chemicals legislation is sometimes insufficient to adequately assess assumptions about potential risks to humans and the environment. Preparatory research can help to generate effect and exposure data to support and supplement regulatory requirements. Likewise, it should support to develop and test approaches that support safe and sustainable development of AdMat and their applications. Regulatory applied research should systematically investigate the need for specific regulatory measures and should support validation, standardisation and harmonisation of testing and assessment methods.

9 AdMat – Specific examples

9.1 Identify advanced polymers requiring registration

Polymers play an important role for the development of AdMat. They find application e.g. as composite materials (e.g. to advance construction material like concrete), as material for additive manufacturing or for medical applications. Advanced polymers can come along with intended functionalities like electro-activity, magneto-activity, self-repairing or as co-polymer including new types or combinations of monomers and specific structuring (which can also lead to a changed use pattern of conventional polymers). There are also synthetic polymers which mimic natural occuring biopolymers (e.g. synthetic RNA or DNA) or which are made from natural sources or by natural processes (e.g. nanocellulose).

As for conventional polymers, possible concerns associated with advanced polymers are persistence in the environment, release of hazardous substances or potentially problematic micro- and nanoplastics, formation of degradation products of concern as well as barriers for recycling.

In contrast to specific sectoral product regulations (e.g., food contact materials), so far there are no registration obligations or data requirements for polymers under REACH. Current REACH obligations are limited to monomers. In the light of the concerns associated with polymers mentioned above, this leads to an insufficient data base to adequately inform on fate and hazards of polymers. A revision of the information requirements for polymers is considered necessary. This issue has been taken up in the Chemicals Strategy for Sustainability of the European Commission (2020a).

During the last years, the European Commission conducted several reports in accordance to Article 138(2) of REACH[36] and based on the outcome of the second REACH review in 2018 (European Commission 2018) to investigate the necessity and affordability of registration and information requirements for polymers. One task of the work has been the identification of criteria under which conditions polymers can be considered as so called Polymers of Low Concern (PLC) or reversely, the identification of a set of criteria, that can reasonably be assumed to display some hazardous properties for so called Polymers Requiring Registration (PRR). **From the perspective of AdMat, criteria of PLC or PRR have to be designed in a way that it is possible to capture also the possible concerns related to advanced polymers**, for example with regard to a possible release of respirable fibre dusts**. Also strategies have to be developed to account for synthetic biopolymers.**

Specific methods for the testing of hazard and fate of polymers are not yet available. Thus, **standard methods need to be developed just like testing and risk assessment strategies for polymers.** When developing such test methods and test strategies possible further needs for the assessment of advanced polymers should be taken into account.

9.2 Develop strategies to foster safe and sustainable additive manufacturing

Additive manufacturing, colloquially called rapid prototyping or 3D printing, are manufacturing processes where components are constructed layer by layer from a raw material. Additive manufacturing is growing in importance not only in various industrial applications but also for professional users, consumers and in education. It opens new possibilities for design and thus,

[36] on the possibility of the Commission to present legislative proposals as soon as a practicable and cost-effective way of selecting polymers for registration is established (European Commission 2020c)

new manufacturing processes e.g. without subtractive processes like milling, drilling and turning. It is also possible to generate complex composites and geometrically complex structures that cannot be realised by conventional production processes. In its trend report of 2018, UBA estimated an annual growth of the global market related to 3D print of about 45%, reaching 17,2 billion US dollar in 2020, and 5,6 million devices in use in 2019. The by far largest part are desktop systems (Keppner et al 2018). Additive manufacturing enables decentral operation and an easy supply of e.g. spare parts which can reduce transport efforts and can facilitate reparability. Therefore, additive manufacturing enables new business models, new products and supply chains. Anyhow, additive manufacturing is accompanied by various uncertainties also related to chemical risk.

For additive manufacturing various techniques are available. Most of them are only of industrial relevance (e.g. powder based) while other are also used for non-industrial applications (e.g. filament based). The various techniques and applications result in different risk scenarios. Depending on the individual technique, diverse raw materials are used like powders and filaments (often with unknown, diverse, and potentially hazardous composition), diverse polymers including nanomaterials and modified polymers, diverse metals including metal-matrix-composites but also ceramics, wood, and others. As prices for the technique and raw materials are expected to be decreasing, it is likely that the use also in non-industrial application (and with additional techniques) will further increase.

Potential concerns related to additive manufacturing depend on the raw materials used. In case of insufficient extractor hood or the use of wrong settings volatile organic compounds, (nanoscaled) solid compounds, plasticisers, flame retardant and momomers may be emitted during the printing process. Furthermore, post-treatment processes like polishing, abrasion and cleaning of the printed product can also lead to emission into air or waste water. Other aspects of concern related to 3D printed products are additional information loss about materials/substances along the supply chain (use pattern), additional barrier for recycling and reparability (due to complexity of structure or composition), and open questions regarding durability of printing products (e.g. release of components, mechanical safety during use phase).

According to the directive on general product safety 2001/95/EC (EC 2001c), the manufacturer of a product is responsible for the safety of his product. Even private users become manufacturers or distributors and are responsible for the safety of the printed item when they sell them to others[37]. Often these persons are not aware about their status or even less about their responsibility. Furthermore, they are most probably incapable to assess the safety of their product and to collect relevant data. Substance-related limit values can also be exceeded at commercial and industrial workplaces if strict protective measures are not taken[38].

For a safe use of additive manufacturing, stategies have to be developed that comprise the following aspects:

- Measures (e.g. thresholds, information on proper use, eco-label) need to be established that promote the development and use of low-emission printers, printing materials that are free of hazardous substances and materials, and mechanically safe printing products that do not release hazardous substances during the life cycle. These measures should also include possibilities to improve the information sharing along the supply chain of the printing material to e.g. facilitate data availability for regulatory risk assessment.

[37] BAuA website on product safety with 3D printing: https://www.baua.de/EN/Service/Publications/Guidance/3D-printing.html
[38] BAuA website on research on determination of hazardous substances exposure during additive manufacturing: https://www.baua.de/EN/Tasks/Research/Research-projects/f2410.html

- Methods for a standardised measurement of emissions during additive manufacturing need to be developed and established.
- Although additive manufacturing promises benefits in the sense of reduced resource consumption, there are considerable concerns about the negative impact on recyclability due to the new possibility of producing complex structures and compositions of printed products and the loss of information along the supply chain. Waste collection and recycling options have to be developed to overcome that obstacle.

9.3 Managing health risk of fibres

Fibrous and fibre-containing materials are currently in the spotlight of innovation due to their technological advantages. In addition to the efforts to improve thermal insulation, which are being stepped up for climate protection reasons, this applies above all to the development of lightweight construction materials. Both fields of application are generally associated with large production volumes and a wide range of uses, so special attention must be paid to the protection of human and environment. Driven by the tragedy of the fibre material asbestos, which have not yet been overcome, and the 3D principle of fibre toxicology, which has been established since the 1970s, special attention must be paid to advanced fibrous and fibre-containing materials.

Health risks are only to be assumed if a material releases a relevant amount of respirable and biopersistent fibre dust during extraction, production, treatment and processing up to disposal or recycling. This applies above all to occupational safety and health in the life cycle of the materials. Since only fibres with diameters below approx. 3 µm can reach the deep lungs, the risk characterisation can be focused on materials with correspondingly small fibre diameters. However, there are also a few known cases, e.g., p-aramid or certain pitch-based carbon fibres, in which respirable fibre dust can also be released from thicker fibres, e.g., by longitudinal splitting under mechanical stress. The length of the inhaled fibres is also relevant to the health risk; it must be greater than approx. 5 µm to cause damage due to the fibre principle. The third important parameter is high biopersistence, i.e., the fibre dissolves only slowly or not at all in the lung environment, which means that repeated exposure may lead to long-term accumulation.

The assumption that extremely thin nanofibre materials pose a particularly high risk has not yet been confirmed. In fact, entangled carbon nanofibres with diameters below 30 nm only show the significantly weaker adverse effect of granular particles. Thicker fibres, on the other hand, feature a clear carcinogenicity in relevant animal experiments. It is assumed that in addition to the influencing factors already outlined, the rigidity of the respirable fibres plays an important role. The German proposal for a harmonised classification of multiwalled carbon nanotubes (MWCNT) takes this consideration already into account and proposes a classification for fibres with diameters above 30 nm. However, the toxicological effects of smaller fibres, especially those that can form bundles still require a detailed investigation.

A further problem in risk assessment arises from the fact that the counting conventions for workplace measurements, which are based on asbestos assessment, do not take into account fibres with diameters below 200 nm. BAuA is currently working on a corresponding extension of the measuring method, which, however, for statistical reasons, no longer permits manual counting of the scanning electron microscope images of the sample carriers. AI-supported automated evaluation procedures are therefore an integral part of this development.

A testing and evaluation strategy tailored to assess the health risks related to fibre dusts is currently not implemented in European chemical safety legislation. For example, it has long been known that the inhalation studies in rats foreseen under REACH may lead to false negative results due to a too low sensitivity to fibre dusts. The much more sensitive tests with

intraperitoneal application for carcinogenicity or intratracheal application for biopersistance have been included in the CLP Regulation for the harmonised classification of mineral wool. However, scientific knowledge suggests that these standardised methods are also more widely applicable to other advanced fibre materials.

Against the background of the rapid developments in the field of AdMat, these regulatory gaps need to be closed, especially in order to improve the data basis for risk assessment at workplaces. Methods for identifying materials with critical fibre diameter are also derived from the classification of mineral wool and ceramic fibres and are already laid down in the European Test Methods Regulation (EC 2008b) and are likely to be transferable to other types of fibres. A dustiness test, developed by BAuA and designed for detection of "critical fibres" is ready for standardisation to provide a low-cost contribution for the prediction of possible exposure during the life cycle of the fibre material. If necessary, this test may enable waiving of later toxicological tests, which are only useful in the case of a health-relevant potential for release of fibre dust.

The next planned step is **a systematic analysis of risk management options (RMOA) including existing regulations.** For this purpose, it is assessed which fibre materials are currently on the European market. The main starting point is the presence of fibres with a respirable diameter. However, this does not yet allow to draw any conclusions about a possible health risk. The aim is to **establish a regulatory framework that ensures both the generation of reliable use and exposure data and their comparison with quality-assured data on morphology, biopersistence, effect and potency** - as a contribution to a material development that meets the claim of being "safe and sustainable".

9.4 Ensure safe use and proper waste management of active and intelligent packaging

The principal function of packaging is to protect products from damage during transport, contain the products or to promote and display the products. Products are therefore packaged directly after manufacturing to protect them for example from mechanical damage, dust, oxygen, light, microorganisms, spoilage or moisture. Active packaging should also actively maintain the quality of the packaged item, e.g. food. Thus, active packaging actively extracts certain substances from the food or its immediate environment (e.g. oxygen from the residual air in the packaging) or releases certain substances - e.g. preservative substances - to the packaged food. If the "active" components are integrated directly into the packaging material, this can be referred to as AdMat. Examples of this are moisture regulating materials such as silica gel or starch polymers, which are located directly in the packaging material. Another example is the use of EcoG+ in cosmetics (SCCS 2016).

A distinction must be made between "active packaging" and "intelligent packaging". The latter monitors the condition of the packaged item and can thus provide information, for example, about the freshness or compliance with the cold chain of packaged food. Here, monitoring of critical limit values (e.g. temperature, time) takes place. Due to the increased manufacturing costs per package, the spread of this form of packaging is still relatively small. Sensor based intelligent packaging can also enable to track goods and opens the possibility to report information along the supply chain up to the customer or end-of-life stage. In this way, damaged packaging, expired or counterfeited products or improper storage and transport conditions can be detected more easily. This technology could facilitate cold chain maintenance for temperature-sensitive products (e.g. medical products) and ensure proper transport conditions for high-end products (e.g. IT technology).

The use and approval of active and intelligent packaging is regulated in the EU by a specific regulation (EC 450/2009) (EC 2009c). However, a **specific guidance for the evaluation of active and intelligent packaging is needed and has to be established**.

Many packaging materials are no longer needed and discarded at the beginning of the use phase of the contained product. From an environmental perspective, packaging should be avoided in the first instance. **Where this is not possible, adverse environmental effects associated with the production, transport and end-of-life treatment of packaging should be minimised as much as possible. Packaging – in particular short-lived packaging - should be designed such as to allow high-quality recycling with a minimum loss of valuable raw materials. This also applies to intelligent packaging.** Potential advantages of active and intelligent packaging, such as light weight, measuring ability and traceability of goods, contrast with potential drawbacks like poor recyclability (e.g. due to physical disturbance of the process, due to accumuation of substances and materials of concern in the material flow), other rebound effects (e.g. more food wastage due to unsaleable goods or premature food disposal), and also potential releases of critical substances or materials of concern into the environment as a result of proper or improper disposal of the packaging.

Therefore, it should be considered thorougly for which kind of application intelligent packaging provides a sustainable benefit in the overall context. For instance, increasing food safety does not necessarily require the use of active and intelligent packaging. Food should be purchased wisely and stored properly. This is the formula to reduce food wastage.

9.5 Specify information needs and develop test strategies for nanocarriers

Nanocarrier and (nano)capsulated active substances are already widely used in medicine and are frequently discussed for application in other areas such as cosmetics, biocides/ pesticides, food and feed (Patra et al. 2018; Camara et al. 2019; EFSA 2020). The aims of these applications are, e.g. improved solubility, targeted release and protection against premature degradation combined with a reduced amount of active substances needed for the application.

Several of the existing legal frameworks for chemicals meanwhile have been updated to specify the information need for nanomaterials (see chapter 3). The information needs for nanocarriers have not yet been specified. Different types of materials can be used as nanocarriers, e.g. nanocapsules, porous silica, hydrogels, micelles/liposomes, dendrimers or electrospun fibres. It should be noted that most of the test methods developed for nanomaterials so far are intended to be used for solid particles while some of the carriers are considered to be non-solid. These non-solid systems may pose several challenges with respect to physico-chemical characterisation, which are not yet adequatly adressed. So far only a few nanocarriers have been assessed. The SCCS, for instance, has assessed a nanoscaled styrene/acrylate copolymer for cosmetics that is intended to be loaded with substances such as methylsilanol mannuronate or dimethylsilanol hyaluronate to offer slow release at the cutaneous level, which is meant to be antistatic, humectant, moisturising and skin conditioning (SCCS 2018; SCCS 2020). The SCCS considered this as a test case for a novel way to use nano-scale substances in cosmetics, which potentially opens up the opportunity for the use of numerous other (bioactive) substances in a large number of applications resulting in a wider exposure of consumers to nanoencapsulated materials. Yet, the safety of such systems has not been assessed adequately. This issue was taken up in the updated SCCS guidance document on the safety assessment of nanomaterials in cosmetics stating that the safety assessment should consider every compound (i.e. the encapsulating material and the cargo) on its own as well as the whole entity (SCCS 2019). However, the detailed information requirements and appropriate test methods are not yet specified. Similarly, EFSA covered the issue of nanocarriers in their updated guidance document

on food and feed, also emphasising that a separate assessment is required for every compound (i.e., encapsulating material and the cargo) as well as for the whole entity (EFSA 2018). Also EFSA does not yet specify the information requirements nor appropriate test methods.

Even in cases, where there might be little or no concern on the carrier itself, the intended use poses challenges. For instance, the durability of the whole entity is very important for the assessment but appropriate test methods still have to be developed. In addition, the carriers may increase the bioavailability of the cargo significantly (some of them are even designed for this purpose) but this is not reflected in the current assessments. Current risk assessments are typically based on external doses. The carrier may also alter the toxicokinetic of the cargo.

For environmental assessments, it needs to be clarified if nanocarrier or nano-encapsulates should be considered either as active substance as a whole or if they present a combination of active substance and co-formulant requiring a separate assessment. With the latter one, a realistic environmental risk assessment seems to be hardly achievable. It needs to be eluciated how fate (i.e., release, transformation, degradation) and effect in the environment of the active substance will be modulated by the encapsulation. The actual reliability of the release control of the carrier or encapsulate needs to be verified in real applications, and especially in cases if unintended release of the product is conceivable.

Therefore, appropriate test strategies, test methods and regulatory information requirements are needed for an adequate assessment of human health and environmental risk potentially posed by nanocarrier systems in the various fields of application.

Summary Chapter 9

Depending on their complexity or intended use, AdMat may provide challenges from a chemical safety and sustainability perspective that differ in quality and quantity and may be of different relevance depending on the object of protection. Some of these challenges are not necessarily new but provide good examples to highlight specific weaknesses, e.g. in regulatory coverage. Other challenges might be new due to new technical applications, functionalities or availabilities, and therefore, may require new measures or the development of adapted methods for assessment and management.

10 Conclusion and main recommendations for action

AdMat are believed to be the basis for many of tomorrow's technologies. They show a great potential to provide technical solutions for the most pressing global challenges we are facing today, e.g. shortage in resources, energy revolution, health care, and environmental pollution. Thus, AdMat and innovative manufacturing processes are in the focus of current innovation research, with anticipated benefits for the economy, the society, and the environment. However, this makes it very challenging to derive which AdMat types we will face tomorrow and to predict to which extent existing regulatory frameworks will be suitable to address their chemcial safety along the life cycle. Furthermore, some AdMat may also pose important challenges regarding further sustainability aspects, including the impact on circular economy.

This document summarises the current perspective of the German Higher Federal Authorities BAuA, BfR , and UBA on AdMat with particular regard on material safety but also further sustainability aspects. It proposes paths forward to a comprehensive framework to address challenges associated with AdMat from a national authorities point of view. The present document should be regarded as a thought starter. The considerations and proposals within this documents will be further discussed with focus on possibilities for implementation in cooperation with other national, European and international stakeholders from science, policy, industry and civil society.

The recommendations made in this document include proposals for action on safe handling and to foster sustainable development of AdMat, and comprise:

- Identifying materials of concern by setting criteria and an early warning system
- Enabling regulatory preparedness and shaping regulations to keep the regulatory framework up to date
- Promoting safe and sustainable design of AdMat
- Supporting stakeholder exchange and co-creation
- Ensuring adequate regulation by enhancing preparatory research and strengthening regulatory research.

In the European context, AdMat can only be considered positive regarding their sustainability, if they provide a positive contribution to the European Green Deal and the corresponding EU Chemicals Strategy for Sustainability, i.e. if beside the benefits also the potential risks for man and environment are identified and appropriate measures for safe handling are taken. However, also beyond Europe, the development of safe and sustainable materials and processes are key to achive a sustainable society. The United Nations Sustainable Development Goals (SDGs – Agenda 2030) set an overall reference framework also for the advancement of materials. The improvement of the overall sustainability of the design, production, use, and end of life of materials are significant to foster the transition to a sustainable society.

11 Profiles of the participating higher federal authorities

11.1 German Federal Institute for Occupational Safety and Health (BAuA)

Safe and healthy working conditions mean social progress and a competitive economy. At the same time, the constantly changing working environment presents new challenges for occupational safety and health on a continual basis.

BAuA explores the conditions and developments in gainful employment with a view to providing workers with the best possible protection and support both today and in the future. Based in Dortmund, Berlin and Dresden with about 720 employees in 2021, BAuA is under the supervision of the Federal Ministry of Labour and Social Affairs (BMAS) and for the Federal Office for Chemicals within the purview of the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU).

BAuA give policy advise on all questions of safety and health at work and the adaptation of working conditions to the needs of humans. As a departmental research institution of the federal government, it acts as a mediator between science, politics and society. BAuA's key tasks include policy advice, the performance of sovereign tasks and the transfer of knowledge into workplace practice. With the DASA Working World Exhibition, BAuA succeeds in conveying to a wide audience the idea of a working environment that is adapted to the needs of humans. Furthermore, BAuA provides comprehensive information and practical solutions for a variety of target group. As a Federal Office for Chemicals, BAuA is the legally competent authority for tasks within the framework of the REACH, the CLP and the Biocides Regulation.

The 4-year programme of BAuA is structured around four strategic priorities:

- Safe-to-use chemicals and products
- Fair and human working conditions
- Prevention of work-related diseases – promotion of health and workability
- Understanding changes to the working world and refining occupational safety and health governance

11.2 German Federal Institute for Risk Assessment (BfR)

The German Federal Institute for Risk Assessment (BfR) was established in November 2002 to strengthen consumer health protection. It is the scientific institution of the Federal Republic of Germany that prepares opinions and expertises on questions of food and feed safety, as well as the safety of substances and products. The main tasks of the BfR comprise the evaluation of existing risks and the identification of new ones, the preparation of recommendations on risk limitation and the communication of this process. This work flows into the scientific advice given to political decision-makers.

The main areas of work are laid down in the "Act restructuring consumer health protection and food safety" of 14 August 2002 and encompass the

- health assessment of biological and material-chemical safety of food,
- health assessment of the safety of substances (chemicals, pesticides, biocides) and selected products (consumer products, cosmetics, tobacco products, textiles and food packaging),
- risk assessment of genetically modified organisms in food, feed, plants and animals,

- risk communication and
- the development and validation of alternative methods to animal experiments.

The BfR has three locations in Berlin and currently has 1 153 employees (2020).

The BfR also conducts own research on topics, which are closely related to its assessment tasks in consumer health protection and food safety. The applied safety research for nano- and other advanced materials is one of these topics, where the BfR participates in numerous national and international third-party funded projects. Current research focuses on the establishment of grouping approaches for the toxicological assessment of nanomaterials, the development of screening procedures for nanomaterials based on (surface) reactivity, and the development of alternative and, in particular, data-driven (in-silico) methods to improve the predictability of the toxicological potential of nanomaterials. Additional research activities focus on nano-specific modes of action.

Furthermore, the BfR also contributes to the development and amendment of legal procedures, in addition to relevant technical guidance for chemicals in nanoform (e.g. the adaptation of OECD test guidelines and guidance documents). The BfR is also represented in relevant expert committees such as the ECHA Nanomaterial Expert Group, the EFSA cross-cutting working group on Nanotechnology, the Scientific Committee on Consumer Safety (SCCS) and the OECD Working Party for Nanomaterials (WPMN).

11.3 German Environment Agency (UBA)

The mission statement of the German Environment Agency (Umweltbundesamt/UBA) is “For our environment” (“Für Mensch und Umwelt”). Founded in 1974, UBA is Germany’s central environment agency within the purview of the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU). Its main statutory responsibilities are as follows:

- Scientific support for the Federal Government
- Enforcement of environmental law (such as on emissions trading, authorisation of chemicals, biocides, pharmaceuticals and plant protection products)
- Protection of human health from environmental pollution, and health-related environmental monitoring
- Public information on environmental protection

Identifying tomorrow’s problems today: The UBA regards itself as an early warning system that provides timely detection of potential future impacts on humans and the environment, assesses them and proposes practicable solutions with the objective of sustainable development. For this purpose, UBA experts carry out research in the agency’s own laboratories and award research contracts to scientific institutions in Germany and abroad. The UBA acts as partner and Germany`s focal point to numerous international organisations such as the WHO. It works closely together with global bodies, institutions and state entities, for example in Europe, the USA and Asia.

Organised in five divisions and a general services division, the UBA employs a staff of some 1,600 at 15 locations, including seven stations in its air quality monitoring network.

The UBA actively contributes towards providing information about environmental aspects of nanotechnology, closing knowledge gaps and identifying further needs for action. Current main focus is on supporting the amendments of legal requirements to nanoforms of substances as well

as the development of harmonised test methods for nanomaterials (i.e. OECD test guidelines and guidance documents). In order to support the discussion on considerations of the special features of nanomaterials in national, European and international chemical safety, UBA is taking an active part in *inter alia* the ECHA Nanomaterial Expert Group as well as the OECD working Party on Manufactured Nanomaterials (WPMN) to provide regulatory guidance. The activities in nanomaterials are currently broadened to also take into account further AdMat.

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