WP2 Case Study

Nanotechnologies

The RECIPES project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 824665

Authors

André Gazsó, Institute of Technology Assessment, Austrian Academy of Sciences

Anna Pavlicek, Institute of Technology Assessment, Austrian Academy of Sciences

Contributors

Gloria Rose, Institute of Technology Assessment, Austrian Academy of Sciences

Sabine Greßler, independent scientist (funded by NanoTrust at ITA-OAW)

Rene Fries, independent scientist (funded by NanoTrust at ITA-OAW)

With thanks to:

Thanks to all RECIPES partners for valuable input and discussion, especially partners at Maastricht University, The Danish Board of Technology, Rathenau Institute, and Humboldt University

Manuscript completed in [September, 2020]

Document title	Case Study on Nanotechnologies
Work Package	WP2
Document Type	Deliverable
Date	10 09 2020
Document Status	Final version

Acknowledgments & Disclaimer

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under grant agreement No 824665.

Abstract

Nanotechnology has been established as a new field of interest at the beginning of the new century to foster interdisciplinary research and bringing together different scientific disciplines and approaches such as material physics, life sciences and toxicology. As an emerging technology and an important group within the so-called advanced materials, nanotechnologies are characterized by manifold areas of application and high uncertainty. The European Commission pointed out that nanotechnologies and nanosciences will offer promising solutions for a wide variety of technical problems in a socially acceptable and environmental-friendly way. Therefore, the nanotechnology research programmes have been associated by safety and sustainability research from the very beginning. National nanotechnology research strategies and action plans followed this policy very soon. Moreover, it has been emphasised that a transparent public communication and a serious inclusion strategy has to be applied to inform the interested public and all concerned parties about the benefits but also about possible disadvantages of these new materials and products. Additional to the nanotechnology research programmes most of the member states opened calls for safety issues mainly focussing on worker safety, consumer protection and toxicology. The European Commission and the European Parliament debated and published detailed nanospecific regulation on topics of high concern like cosmetics, novel food and food contact materials at an early stage. Finally, these activities were carried out by establishing national and international networks to include all relevant knowledge. This tight interaction between organising and evaluating the available knowledge on nanotechnologies and their effects on different systems, translating and disseminating these results on possible benefits and adverse effects to all interested parties and setting up specific communication and working processes such as nanotechnology commission in Austria are an illustrative example how the precautionary principle and its following concepts like responsible research and innovation can be successfully applied.

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List of abbreviations

AG	Silver
AFNOR	Association française de normalisation (French standardisation authority)
ANSES	Agence nationale de sécurité sanitaire, de l'alimentation, de l'environnement et du travail (France)
ASI	Austrian Standardisation International
AUVA	Allgemeine Unfallversicherungsanstalt (Austria) – Austrian Workers' Compensation Board
BfR	Bundesinstitut für Risikobewertung (Germany)
BSI	British Standards Institution
CA	Consortium Agreement
CC	Consortium Committee
Cd	Cadmium
CdTe	Cadmium Teluride
CdSe	Cadmium Selenide
CEN	European Committee for Standardization (Comité Européen de Normalisation)
CNT	Carbon nanotube(s)
DIN	Deutsches Institut für Normung (German standardisation authority)
DOA	Description of Action
ECHA	European Chemicals Agency (EU)
EC	European Commission
EFSA	European Food Safety Agency (EU)
EHS	Environmental, Health and Safety
ENM	Engineered nanomaterials
ENP	Engineered nanoparticle
EUON	European Union Observatory for Nanomaterials
FCM	Food contact material(s)
GA	Grant Agreement

IRGC	International Risk Governance Council
ISO	International Organization for Standardization
ITA-OeAW	Institute of Technology Assessment, Austrian Academy of Sciences
KET	Key enabling technology
MWCNT	Multi-walled carbon nanotube(s)
NBIC	Nanotechnology, Biotechnology, Information technology and Cognitive science (part of the so-called "converging technologies")
NIOSH	National Institute for Occupational Safety and Health (US)
N&N	Nanotechnology and nanosciences
NOM	Natural organic matter
ÖAW	Österreichische Akademie der Wissenschaften - Austrian Academy of Sciences
ÖNAP	Österreichischer Aktionsplan Nanotechnologie (Austrian Action Plan Nanotechnology)
OSHA	Occupational Safety and Health Authority (EU)
PCG	Project Coordination Group
PO	Project Office
PV	Photovoltaic
QD(s)	Quantum Dot(s)
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
ROS	Reactive Oxygen Species
RRI	Responsible Research and Innovation
SbD	Safe-by-Design
SDG	Sustainable Development Goal(s)
SCCP	Scientific Committee for Consumer Products (EU)
SCENIHR	Scientific Committee on Emerging and Newly-Identified Health Risks (EU)
TC	Technical Committee
TiO_2	Titanium dioxide
WP	Work Package

1 Introduction

1.1 Introduction

The term nanotechnology (as singular) has been introduced by several reports by the US National Science Foundation which strived to establish a new and attractive research field at the end of the 1990ies. This happened mainly in the wake of the winning of the Nobelprice for chemistry 1996 by Richard Smalley (together with Robert F. Curl and Harold Kroto) for their seminal work on fullerenes. As a consequence, there were certain hopes to revitalise research in several fields such as material physics, powder metallurgy or polymer chemistry. From an early stage on these scientific attempts were accompanied by intensive discussions on societal, economic and ethical considerations. The main focus of the US-American debate lay on the development of new materials, especially for the use in automotive and aerospace applications, but also on medical applications (diagnostics and drug delivery) including the improvement of human performance [1].

Nanomaterials range from 1-100nm in size and can be found in the form of platelets, fibres or particles. They can occur naturally, or they can be manufactured deliberately to benefit from the novel functionalities which nanomaterials exhibit as a result from their increased surface-to-volume ration and subsequent higher reactivity of particle surfaces. The commercialization of such synthetic nanomaterials or "engineered nanomaterials" (ENMs) began in the early 2000s but neither short-term nor long-term potential consequences for human health and the environment are sufficiently known [2]. Nanotechnology is considered a key technology of the 21st century with an annual market growth of up to 20.7%. It represents a very complex and multifaceted topic, the term being an umbrella for a multitude of products and processes rather than a single technology or application, simultaneously being regarded as an "emerging technology" as well as an "emerging issue of environmental concern" [3].

New nanomaterials or -products can have a high degree of potential beneficial uses resulting from their new functionalities, but at the same time they are characterized by high uncertainty, which entails unpredictable risks. When faced with uncertainty, valid data for the level of damage and probability of occurrence cannot sufficiently be provided, which hinders risk assessments and confronts regulators with the situation that there is lacking evidence to base decisions upon. At the same time, the increasing use of engineered nanomaterials (ENMs) in products and applications, ranging from electronics and automotive technology to consumer products and environmental technology [4][5][6], leads to an increased likelihood of exposure of humans and the environment, as ENMs can be released at different stages of their life cycle - during production, processing, use or disposal [7][8]. Seeing as adverse effects, biological interactions and toxicity mechanisms are not comprehensively understood, they can also not be excluded [9][10]. Faced with these circumstances, several public authorities on EU as well as on national level have chosen to apply the precautionary principle (PP) and explore governance approaches with strong interdisciplinary, cooperative and network-oriented elements over the past decade.

In the case of the extraordinary diverse field of nanotechnology, it became apparent very quickly that risk and safety issues were not or at least not sufficiently addressed under the existing regulatory regimes (food safety, workplace safety, chemical regulation) and the existing approaches to hazard identification, evaluation and risk management. Therefore, traditional exposure and risk assessment (including e.g. modelling or testing approaches) were not applicable for nanomaterials and risks for human health and/or the environment could not be estimated.

From an early onset the European Commission (EC) propagated an "integrated and responsible approach" on nanotechnology in its Nanoscience and Nanotechnology Action Plan of 2005 based on the precautionary principle [11]. Simultaneously, it strives to

integrate innovation and sustainability (safety being one important aspect of sustainable development) by requiring the provision of favourable conditions for industrial innovation on the one hand and the respect of ethical principles, integrate societal considerations into the R&D process at an early stage. In chapter 5 and 6 of its Action Plan, after discussing issues of research policy and educational prerequisites in the previous chapters, the EC states that an essential element of a responsible strategy for nanotechnology research will be to integrate health, safety and environmental aspects to the technological development and to establish an effective dialogue with all stakeholders. This will be based on three cornerstones, i.e. the advancement of an independent nanotechnology risk research, the establishment of a transparent public communication strategy on nanotechnologies and the support of national and international network building on risk and safety issues regarding the development and use of nanomaterials and nanotechnologies. Several national nanotechnology action plans were to follow this outline, such as Germany (2006), Switzerland (2008) and Austria (2010).

It is not really a surprise that the application centred debate on nanotechnologies which has dominated the US-American discourse was very soon focused on health and safety aspects, mainly gathered around risk and precautionary aspects. This realignment of the driving concepts behind the development of nanotechnologies started very early during the establishment of the national nanotechnology research programmes, e.g. the NanoInitiative in Austria. Secondly, the public discussion about the development and use of nanotechnologies was concentrating on the use of nanomaterials and production processes rather than on nanotechnologies and finally the discussion moved through the years out of the public sphere and has been active since in professional discourse dealing with e.g. food and workplace safety. The main topics chosen were the most commonly used substances (such as nanosilver, titanium dioxide or carbon nanotubes) and their incorporation into everyday products, such as compound materials, special paints and varnishes, food, cosmetics and functionalised textiles. This kind of "normalisation" of the discourse by establishing appropriate expert panels and specific commissions (i.e. the Austrian Nanoinformation Commission of the Federal Ministry of Social Affairs) accompanies the nano research and development since at least one decade.

1.2 Key timeline

The timeline below presents key events, political or legal events or decisions, implementations of legal frameworks, the most crucial scientific findings and risk assessments, and selected public debates. The different categories of actions are visualised by different colours.

Political	*Legal*	*Science/risk assessment*	*Public debate*	*Other*

Year	Event	Relevance to case study
1997	5th Research Framework Programme (FP5) 1998 – 2002 [12]	First mention of nanotechnology within an EU-level strategic document
2000	Communication from the Commission on the precautionary principle [13]	
2002	6th Research Framework Programme (FP6) 2002-2006 [14]	First research projects on EHS-issues regarding the use of nanotechnologies

Political	*Legal*	*Science/risk assessment*	*Public debate*	*Other*

Year	Event	Relevance to case study
2003	Start of the Austrian nanotechnology research programme NanoInitiative	The Austrian NANO Initiative is a multi-annual funding programme for Nanoscale Sciences and Nanotechnologies (NANO) in Austria and is focused on applied research and public outreach projects (mainly funded by the Ministry of Traffic, Innovation and Technology). First discussions on risk and safety issues to be integrated into nanotechnology F&E
2004	Communication from the EU Commission - Towards a European strategy for nanotechnology [15]	This Communication proposes actions as part of an integrated approach to maintain and strengthen European R&D in nanosciences and nanotechnologies. It considers the issues that are important to ensure the creation and exploitation of the knowledge generated via R&D for the benefit of society
2005	Report "Nano 2005 – 2006" (BMVIT) by the Institute of Technology Assessment (ITA) at the Austrian Academy of Sciences [16]	The Ministry of Technology begins to draw its attention to environmental, health and safety topics regading nanotechnologies
2005	Action Plan for Europe 2005 – 2009 for nanosciences and nanotechnologies [11]	An essential element of this responsible strategy is to integrate health, safety and environmental aspects to the technological development of nanotechnologies and nanosciences
2006	Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency [17]	REACH is the over-arching legislation applicable to the manufacture, placing on the market and use of substances on their own, in preparations or in articles. Nanomaterials are covered by the definition of a "substance" in REACH, even though there is no explicit reference to nanomaterials. The general obligations in REACH, such as registration of substances manufactured at 1 tonne or more and providing information in the supply chain apply as for any other substance. Information on the implementation of REACH for nanomaterials, including guidance and the application of the REACH evaluation processes, can be found on the ECHA website.
2007	7th Research Framework Programme (FP7) 2007 – 2013 [18]	Nanosafety projects on workplace safety, cell biology and environmental toxicology
2007	Federal Chancellery Austria: Decision of the Bioethics Commission at the Federal Chancellery of 13 June 2007 – Nanotechnology Catalogue of ethical problems and recommendations [19]	Considering the precautionary principle, the main question for the political discourse is whether the legislator should develop a special legal framework (analogous to the Genetic Engineering Act) or whether it should limit itself to active research policy and/or information policy towards the population. The Bioethics Commission acknowledges the fact that there is a gap of knowledge regarding the dangers of nanotechnology, but believes that a sufficient risk-benefit balance, both for the medical sector and for the food and technology sector, will be ensured within the existing authorization procedures. Nevertheless, the Bioethics Commission recommends within the framework of the public-sector research policy, both risk research and the intensify accompanying research, including ethics.

Political	*Legal*	*Science/risk assessment*	*Public debate*	*Other*

Year	Event	Relevance to case study
2007	Nano safety Project: NanoTrust 2007 – 2010 at the ITA (Austrian Academy of Sciences)	In Austria NanoTrust project of the Institute of Technology-Assessment (ITA) at the Austrian Academy of Sciences (ÖAW) is launched. The main goals of the project are to identify scientific needs in nanosafety research and to provide an independent platform for discussion on nanosafety issues
2007	Behördendialog (Dialogue of Authorities)	The "Behördendialog" is held for the first time as a German speaking platform for knowledge exchange on nanosafety issues, initiated by the German Ministry of Environment (BMUB), the Swiss Ministry of Health (BAG) and the Austrian Ministry of Environment (BMLFUW). It will take place annually in in one of the member countries (D, A, CH; FL and LUX will follow a few years later). It will take place for the 14th time in November 2020.
2008	EC Communication on Regulatory aspects of nanomaterials [20]	The Commission announces a regulatory review of EU legislation in relevant sectors. The present Communication reflects this commitment. It covers nanomaterials currently in production and/or placed on the market
2008	Food Additive Regulation (Regulation No. 1333/2008) [21]	Regulation (EC) No. 1272/2008 on classification, labeling and packaging of substances and mixtures CLP [13]
2008	European Parliament Resolution of 24 April 2009 on regulatory aspects of nanomaterials [22]	The European Parliament in its resolution of 24 April 2009 on regulatory aspects of nanomaterials called, inter alia, for the introduction of a comprehensive science-based definition of nanomaterials in Union legislation
2009	Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products [23]	First nanospecific law introducing a working definition for nanotechnologies
2009	EU Commission Recommendation on a code of conduct for responsible nanosciences and nanotechnologies research [24]	Code of conduct on a voluntary basis for the use in nanoproduction
2010	Austrian Actionplan for Nanotechnology (ÖNAP) [25]	Consisting of 50 recommendations regarding the safe and sustainable use of nanotechnologies and nanomaterials which are still implemented (EHS research programme, nanoinformation web site, nanoinformation commission)
2010	Report: Nanotechnology in Vienna's procurement system - initial assessment of opportunities and risks [26]	This paper is intended to give decision-makers within the procurement system of the Municipality of Vienna a brief overview of products and applications attributed to nanotechnology, especially with regard to their propagated environmental benefits and their potential risks for health and the environment. Priority will be given to those product groups that are available on the Austrian and European market and that are important in the procurement of the municipality of Vienna.
2010	Establishment of the Austrian Nano Information Platform (NIP)	Lead by the Austrian Ministry of Health, consisting of members from various organisations (ministries, agencies, research institutions, NGOs)

Political	*Legal*	*Science/risk assessment*	*Public debate*	*Other*

Year	Event	Relevance to case study
2010	ITA Project: NanoTrust 2 – 2010-2013 (BMVIT)	First prolongation of the long-term research project on nano risk governance at the Austrian Academy of Sciences
2010	EU Commission: Eurobarometer Biotechnology – Awareness of Nanotechnology [27]	The key findings of this survey are that Europeans are generally unaware of nanotechnology, do not have a solid view of benefits but are not excessively alarmed about potential negative consequences. Even though understanding of nanotechnology is low, Europeans feel that it should be encouraged. [20]
2011	EU Commission Recommendation on the definition of nanomaterial [28]	
2011	Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers [29]	amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004
2011	Regulation (EU) No, 10/2011 on plastic materials and articles intended to come into contact with food [30]	First nanospecific regulation concerning food packaging materials
2011	Austrian research programme "Sparkling Science" - Youth research on opportunities and risks of Nanomaterials [31]	In this research project, under the direction of the Federal Environment Agency, high school students from Vienna and Salzburg dealt comprehensively with the perception of nanotechnology
2011	Directive 2011/65 on the restriction of the use of certain hazardous substances in electrical and electronic equipment [32]	As soon as scientific evidence is available, and taking into account the precautionary principle, the restriction of other hazardous substances, including any substances of very small size or with a very small internal or surface structure (nanomaterials) which may be hazardous due to properties relating to their size or structure, and their substitution by more environmentally friendly alternatives which ensure at least the same level of protection of consumers should be examined
2011	Establishment of a permanent working group "Nanotechnologies and Workplace Safety" by the Austrian Workers Compensation Board under participation of the ITA	This working group is active until today (2020) and meets on a regular basis
2012	Regulation (EU) No. 528/2012 concerning the making available on the market and use of biocidal products [33]	The Biocidal Products Regulation contains specific provisions for nanomaterials
2012	The Austrian Workers Compensation Board (AUVA) Code of practice: Nanotechnologies – Health and Safety at Work [34]	Nanomaterials in the workplace are completely different working materials with different physical, chemical and toxicological properties. It is therefore important to provide workers with as much specific information as possible, through training and instruction, about the substances used, the tasks they perform and the processes that may lead to inhalation, dermal or oral exposure

Political	*Legal*	*Science/risk assessment*	*Public debate*	*Other*

Year	Event	Relevance to case study
2012	Austrian Nanotechnology Action Plan - Implementation Report 2012 [35]	In adopting the Austrian Nanotechnology Action Plan on 2 March 2010, the Federal Government provided a clear mandate for its implementation and required the presentation of a progress report on the Plan's implementation by the end of 2012
2012	Directive 2012/19 (EU) on waste electrical and electronic equipment (WEEE) [36]	First systematic considerations of the fate and behaviour of nanomaterials in waste streams
2012	NanOpinion (EU-FP7) 2012 - 2014	
2013	Austrian Nano Information Commission (NIK) at the Austrian Ministry of Health, first term of office	In order to intensify and consolidate the transdisciplinary risk evaluation and communication processes between ministries, authorities and science, the Austrian Nano Information Commission (NIK) was founded in 2013. ITA has been appointed to chair the Commission
2013	ITA Project: Nano Trust 3 – 2013-2016 (BMVIT, BMLFUW, BMG, BMASK)	2nd prolongation of the long-term nano risk governance project "NanoTrust" at ITA, supported by several ministries and the Austrian workers compensation board (AUVA)
2013	German Federal Ministry for Risk Assessment: Nanoview [37]	Factors influencing the perception of nanotechnologies and target group-specific risk communication strategies
2013	European Commission: Guidance on the protection of the health and safety of workers from the potential risks related to nanomaterials at work.[38]	Guidance for employers and health and safety practitioners
2014	Horizon 2020 Framework Programme 2014-2020 [39]	
2013	European Commission: Working Safely with Manufactured Nanomaterials [40]	Guidance for Workers
2015	Regulation (EU) 2015/2283 on novel foods [41]	To ensure a high level of protection of human health and consumers' interests, food consisting of engineered nanomaterials should also be considered a novel food under this Regulation
2016	ITA Project: Nano Trust 4 – 2016-2017 (BMVIT, BMLFUW, BMGF)	3rd prolongation of the long-term nano risk governance project NanoTrust at ITA, supported by several ministries and the Austrian workers compensation board (AUVA,)
2017	Regulation (EU) 2017/745 on medical devices [42]	There is scientific uncertainty about the risks and benefits of nanomaterials used for devices. In order to ensure a high level of health protection, free movement of goods and legal certainty for manufacturers, it is necessary to introduce a uniform definition for nanomaterials based on Commission Recommendation 2011/696/EU (4), with the necessary flexibility to adapt that definition to scientific and technical progress and subsequent regulatory development at Union and international level. In the design and manufacture of devices, manufacturers should take special care when using nanoparticles for which there is a high or medium potential for internal exposure. Such devices should be subject to the most stringent conformity assessment procedures. In preparation of

Political	*Legal*	*Science/risk assessment*	*Public debate*	*Other*

Year	Event	Relevance to case study
		implementing acts regulating the practical and uniform application of the corresponding requirements laid down in this Regulation, the relevant scientific opinions of the relevant scientific committees should be taken intoaccount.
2017	ITA Project: Nano Trust 5 – 2017-2020 (BMVIT, BMNT, BMASKG, AUVA)	4th prolongation of the long-term nano risk governance project NanoTrust at ITA, supported by several ministries and the Austrian workers compensation board (AUVA)
2018	Amending Regulation (EC) No 1907/2006 (REACH) as regards Annexes I, III, VI, VII, VIII, IX, X, XI, and XII to address nanoforms of substances	In force since 2018 – it shall apply from 1 January 2020, concerning new and already existing registrations, explicitly addresses nanoforms of substances. For nanoforms, specific minimum characterisation information should be provided as part of the composition information under the substance identification. Particle size, shape and surface properties of a nanoform may influence its toxicological or ecotoxicological profile, exposure as well as behaviour in the environment.
2020	Austrian Nano Information Commission (NIK) at the Austrian Ministry of Health, second term of office (until 2023)	In order to intensify and consolidate the transdisciplinary risk evaluation and communication processes between ministries, authorities and science, the Austrian Nano Information Commission (NIK) was founded in 2013. ITA has been appointed to chair the Commission.
2020	Horizon Europe Framework Programme – 2021-2027	

2 Nanotechnologies

2.1 The field of nanotechnologies

Because of their high variability and universal use nanotechnologies are among so called key enabling technologies (KET), the others being advanced materials, advanced manufacturing and production technologies and biotechnology. KETs are technologies which are meant to retain the competitiveness of the European industries and capitalise on new markets worldwide. Originally part of a cluster called converging technologies (Nanotechnology, Biotechnology, Information technology and Cognitive science (NBIC)), nanotechnologies are now one important part in the field of advanced materials. The developing European research framework programme Horizon Europe will contain nanotechnologies mainly in the cluster "Digital, Industry and Space", the areas of intervention being "manufacturing technologies", "advanced materials" and "emerging enabling technologies". But nanotechnologies and nanomaterials are modifiable in shape, structure and functionality for special purposes that one can expect nanotechology research to be carried out also in other Horizon Europe clusters, such as "Health" (diagnostics and drug delivery), "Climate, Energy and Mobility" (e.g. water treatment and printable batteries) or "Food, bioeconomy, natural resources, agriculture and environment" (indicators for food quality). It is obvious that nanotechnology is not "one" technology but is getting more and more important in a vast majority of technological sectors.

Nanomaterials and products have already found their way into everyday life, being used in consumer goods, construction, pharmaceuticals and chemicals, healthcare, power generation and information technology (see Figure 1). At present, their use and production are increasing rapidly, although much safety-relevant information is still missing, such as whether, how much and when nanoparticles can be released during the product life cycle. To give an example about the diverse field and applications of nanotechnology we give the example of Quantum Dots (QDs) and their specific application possibilities within different technology sectors. Due to their unique mechanical, magnetic, electrical and optical properties they are of interest for a wide range of materials, products and applications. They can foster innovation in various field but depending on use and application, they can be released into the environment during their life cycle and negative effects such as ecotoxicity cannot be excluded [43].

Quantum Dots (QDs) and their specific application possibilities

QDs are fluorescent nanocrystals, the size varies depending on composition and production method and is approximately 2 to 10 nanometers (nm). These synthetically produced nanoparticles such as cadmium teluride (CdTe) or cadmium selenide (CdSe) usually consist of one or more layers of inorganic semiconductors to which organic ligands are attached, which serve for surface modification. By means of surface modification, nanoparticles can be more or less "tailor-made" according to the area of application and desired properties [44]. Due to their small size, among other things, QDs exhibit specific fluorescence, whereby they emit a specific wavelength after excitation with electromagnetic waves. Their characteristic first exciton absorption peak and a very sharp fluorescence peak are particle size dependent and therefore tunable by the reaction time during their synthesis. They are also photochemically robust (photostable) and allow localization at the molecular level and thus the tracking of complex biological processes over a long period of time. Due to this unique optical property, which is mainly due to the size of the nanocrystals, they are used for energy generation in solar cell technology [45][46], environmental analysis methods [47], biomedicine [48] and nanotoxicology[49] as fluorescent markers. For example, it has been shown that QDs can be clearly detected in living cells [50] and in complex media such as waste streams [47] due to their characteristic fluorescent properties. QDs therefore offer great potential as fluorescent markers or so-called tracer materials.

Although the unique properties of QDs make them suitable for a variety of applications, the semiconductors of most QDs consist of compounds with heavy metals, such as cadmium (Cd), and both the uptake of these nanoparticles and the uptake of dissolved Cadmium ions can be toxic. QDs can, for example, be absorbed into the cytoplasm via endocytosis, where their presence creates oxidative stress and causes the cell to produce reactive oxygen species (ROS), which can damage or kill the cell [51]. On the contrary, it is precisely these reactive oxygen species that enable QDs to be used as probes for photodynamic therapy (PDT), whereby tumor cells can be destroyed in a targeted manner. QDs can also accumulate in the body or in individual organs and thus, apart from their toxicity for individual cells or organisms, can reach higher levels of the food chain by means of trophic transfer. This represents a potential danger for the entire food chain, right up to humans. Despite the expected increase in industrial production and the associated increased release into the environment, there is as yet little information about their fate or potential toxicity [52].

Nevertheless, the use of QDs in the electronics industry or for power generation in solar cell technology is increasing. Likewise, QD marking has become a fundamental tool in various fields of research to quantify and localize nanomaterials in cells and complex media and to better understand their endpoints and effects. In order to guarantee more safety in the future and to be able to understand and thus reduce environmental pollution, the development of standardized analysis and measurement methods as well as reference materials is an important step [47]. However, this poses a problem because the statements of the various ecotoxicity tests are currently often contradictory and not reproducible and therefore do not allow general statements at present.

Solar Cell Technology

Photovoltaic (PV) technology in particular offers a future field of application as it needs to be developed very rapidly in order to achieve the Paris climate targets for 2050 (100% electricity generation from renewable energy). Since this goal cannot be achieved by using classical silicon-based solar cells, novel PV technologies are required to offer flexible, ultra-thin and above all lightweight PV modules. Such flexible systems are based, for example, on perovskite silicon tandem solar cells (multi-junction solar cells) or single-junction perovskite QD cells. Perovskite is a mineral that has unique structural properties and in combination with QDs has great potential in solar cell technology. These novel PV technologies therefore also have a high potential to open up new fields of application - beyond classical energy production - for e.g. portable intelligent small devices or sensors.

For example, research is currently being carried out on so-called colloidal perovskite quantum dots to increase the efficiency of perovskite QD solar cells. However, this research is still in its infancy and does not yet come close to conventional silicon-based PV technologies. Today, commercial silicon PV modules typically have an efficiency of more than 19% over an area of one square meter, while small single junction perovskite QD cells only achieve 16.6%.[1] In addition to further improvements in efficiency and stability, the development of high-throughput coating processes and the reduction of material costs are significant challenges for the commercialization of QD solar cells [45]. A further factor is that perovskites often consist of lead-containing compounds that are harmful to the environment and health, so-called halides [46], which can lead to negative environmental effects if accidentally released. Although the lead emitted by such a solar cell is said to

[1] https://www.solarify.eu/2018/04/08/886-effiziente-perowskit-solarzellen/

account for less than 0.3 percent of the ecotoxicity of the entire module[2], it is to be replaced by more environmentally friendly elements in the future.

Biomedicine

Imaging techniques that use fluorescence are widely used and important methods in biomedicine. QDs can be used as fluorescent labels in bioimaging, as experiments on mice show [53]. In recent decades, cell biology, for example, has often worked with short-lived organic dyes such as rhodamines or cyanines. These organic dyes exhibit photon-induced "chemical degradation", so-called "bleaching", which is an unintended and undesirable effect of prolonged exposure to high light intensities. The instability of the organic dyes thus hinders the long-term absorption and also the tracking of the particles in complex biological processes or in complex media. Organic dyes also have a very broad emission spectrum, which makes the detection of several labels at the same time difficult. On the other hand, different QDs can be detected in parallel due to their narrow, symmetrical emission spectrum. However, organic dyes have been in use for so long that there are commercially available functionalized dyes that are already very well characterized and applicable, which is not the case with QDs and has to be determined very precisely from case to case [54].

However, the biocompatibility of the dyes (organic or inorganic) is essential for their biological and biomedical application, whereby coating materials or "capping layers" can modify the surface properties of QDs to give them water solubility, water stability, photostability and biocompatibility. In addition, QDs can also be conjugated with specific peptides, antibodies and other small molecules targeting a specific cell type, cell structure or tissue. Therefore, QDs are increasingly used in medical diagnostics, e.g. as contrast agents. The successful use of QDs for the detection of tumor biomarkers and the imaging of tumor cells has great potential for application in the early detection of cancer and, due to a possible accurate visual tracking, also in tumor elimination [48].

Due to their specific properties, they are also used in cancer therapy. Photodynamic therapy (PDT) is a very promising method for cancer treatment. In this construct, the QDs serve as antennas to absorb light and transfer the energy via energy transfer to the closely linked photosensitizer to initiate the production of ROS, thereby damaging the cell. Photothermal therapy (PTT) is a new technique for cancer treatment in which QDs can efficiently convert light energy into heat when exposed to laser radiation to inhibit the tumor's growth [55].

Due to their unique properties, QDs can play several roles in the development of drug delivery systems. They can serve as a means of monitoring drug delivery and they can act as carriers, which transport the drug to the target site to increase the dose of the drug in the target organ [56].

Environmental analysis methods

It is being investigated whether quantum dots are potentially suitable as detectable and clearly identifiable so-called "nanotracers" to determine the final fate of synthetically produced nanomaterials in environmentally relevant media such as wastewater or landfill leachates. By labelling nanoproducts containing synthetically produced nanomaterials with nanotracers, it would be possible to estimate the potential input into the environment and predict environmental concentrations. Studies show that the unique optical properties of QDs using fluorescence spectroscopic detection methods in complex environmental

[2] https://www.solarify.eu/2018/04/08/886-effiziente-perowskit-solarzellen/

matrices, such as waste samples, make it possible to clearly identify and track [47]. In addition, these nanoscale tracers can be clearly distinguished from naturally occurring nanomaterials due to their spectroscopic "fingerprint" and can be observed over a longer period of time due to their persistence. By tracing the QDs, insights can be gained into how synthetically produced nanomaterials behave in relevant environmental samples over long periods of time. Conclusions can also be drawn about interactions with natural, organic substances such as proteins, fulvic or humic acids, whereby such potential transformation processes in turn play a decisive role in terms of mobility and toxicity [57].

QDs have also been successfully used as highly sensitive and pH-dependent fluorescence probes (biosensors), e.g. to detect dissolved ions in water samples, since their adsorption on the QD surface is very selective [58].

Nanotoxicology

The visualization and quantification of the dose of nanoparticles in organisms as well as in the environment are topics of utmost importance for the toxicological evaluation of nanomaterials. Visualizing the fate of nanomaterials can provide information describing the interaction mechanisms of nanomaterials with biological matter and finally their toxicity. At the same time, the quantification of the dose of nanomaterials is essential for toxicological evaluation in order to establish a relationship between dose and endpoints and to contribute to the development of models and standardised analysis and testing methods. Despite the great advantages, there are still obstacles to this method, such as the choice of the right label, the stability of the bond with the label over time, or the presence of unbound labels in the solution, which can falsify the results. Therefore, the reproducibility of the studies is often not given and standardisation is difficult [49].

However, there is a need for reliable and reproducible results of ecotoxicological experiments to identify, quantify, classify and rank the environmental hazards of nanomaterials and to set environmental predicted no-effect concentration (PNEC) limits. Standardised analysis and test methods are required for this purpose, which can then be used as a basis for regulatory decisions to ensure the protection of the environment from unintended harmful effects [59].

The future increased use of nanomaterials in innovative application areas such as solar cell technology, biomedicine or environmental analysis is a great opportunity but also carries risks due to the high uncertainties that innovative technologies entail. Nanomaterials are already being used in various commercial consumer products, such as electronics, but still very little is currently known about their production volumes, market distribution and their fate and impact over the value chain and life cycle, because valid information is missing. It is therefore essential to further develop reliable, standardised reference materials, robust analysis and measurement methods as well as a harmonized registration system for all nanomaterials. Reliable, scientifically based and legally binding characterization and measurement method as well as a definition and mandatory registration would create data for quantitative risk assessment, which is currently still vague. A proper risk assessment could contribute to transparency and thus trust in nanotechnology, which foster innovation instead of slowing it down. But as long as this isn´t the case, the safety of nanotechnology will always be questioned, although there is often no reason for this.

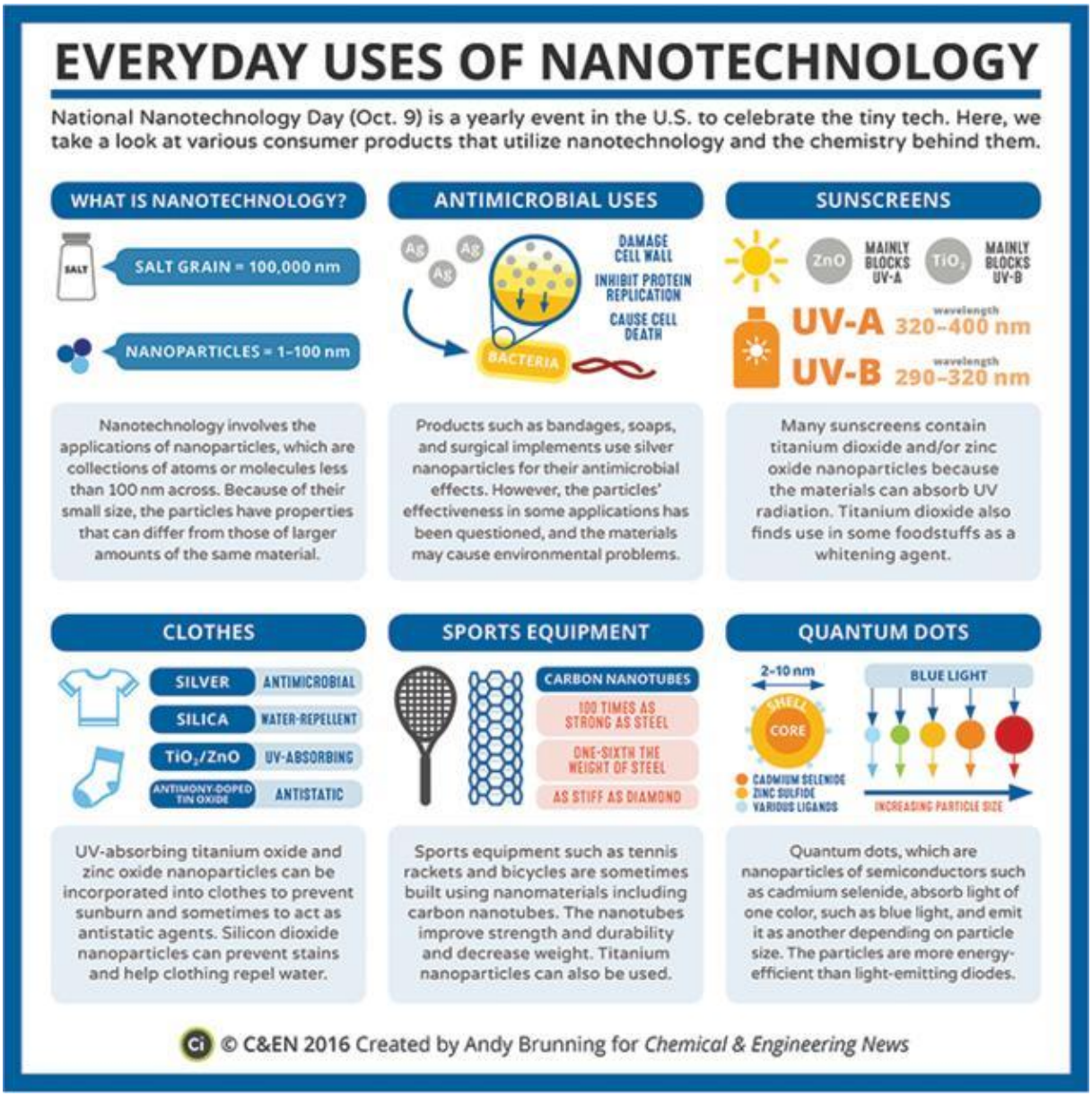

Figure 1 Nanotechnology Uses. [60]

2.2 Precautionary considerations

Because of the high variance of involved disciplines, envisioned scientific problems and possible applications and their innovation level, the transdisciplinarity of the discourse which tried to include a broad variety of stakeholders (research, regulatory bodies and authorities, producers and the interested public (including e.g. civil society and NGO´s)) and the somewhat blurred borders as to what nanotechnologies are encompassing, the EC was eager to open up the interaction between all parties concerned to bring in all safety relevant information as early as possible. In its communication to the Council, the European Parliament and the Economic and Social Committee (Action Plan) the EC emphasises these needs very clearly, especially in points 5 and 6.[61] Following the EC the safe and responsible development of nanotechnologies should be necessarily linked to the integration of the societal dimension and the appropriate assessment of public health, safety and environmental health aspects as early as possible. This needs to be done in a most efficient and effective way by fostering the international cooperation of EHS-research.

The statements of the Commission were clearly based on precautionary considerations. The scientific and technical development of nanotechnologies should be carried out in a responsible manner e.g. via the use of ethical reviews to include possible concerns regarding medical uses. Studies and foresight activities into future nanotechnology scenarios should provide useful information about the possible risks to, and potential impacts on, society. Furthermore, appropriate conditions for and pursue a true dialogue with the stakeholders concerning nanotechnologies should be created. In support of this dialogue, special Eurobarometer (EB) surveys were launched to study the awareness of and attitudes towards nanotechnologies across Member States.

The Commission called upon the Member States to encourage the industry to consider the wider economic, societal, health, safety and environmental impacts of their commercial activities as integral part of their Corporate Social Responsibility strategy [62].

A regular dialogue on nanotechnology application with the public should be opened, in particular via the media. Part of these efforts should be aimed at consumer education projects hoping to raise awareness and – maybe – also the acceptance of these new technologies. Regarding research the EC encouraged the Member States to identify and address safety concerns associated with applications and use of nanotechnologies at the earliest possible stage. The main focus should be the possible exposure to nanoparticles and nanofibers by consumers and workers. The responsible organisations and research institutions should develop guidelines, models and standards for risk assessment throughout the whole lifecycle of nanotechnology products.

As a consequence, several member countries started an open discussion how to deal with the development of nanotechnologies as a society, engaging a great variety of stakeholders. In Austria for example the "Nanonet" of the Ministry of Environment was established, which does not exist in this format today. Subsequently this discourse led to the constitution of a national Action Plans in some Member Countries. Not surprisingly, these national Action Plans contain many of the recommendations such as the establishment of an independent nanosafety research programme, the organisation of a transparent and informative public dialogue (either informal or consultational, but seldomly in a really cooperative manner) [25].

Therefore, the main activities on European and Member State level have been gathered around the research of possible health and environmental effects of nanotechnologies on the one hand, and communication processes on possible effects of nanotechnologies including all conceivable concerned parties.

3 Risks and scientific uncertainties

3.1 Risk/threat and scientific analysis

3.1.1 Human Health Risks

From a toxicological viewpoint a certain risk posed by a substance is connected not only to the adverse effect, but foremost to the exposure of a person or a living being to the respective substance. In the case of nanotechnology, the risk for human health is often identified as occurring at the workplace (including laboratories) where nanomaterials are created or handled. The other group mainly concerned are consumers because they can come into contact with nanomaterials via nanoproducts.

The intake of ENMs can occur through inhalation, dermal absorption or oral ingestion. Furthermore, due to their small size and large surface-to-volume ratio, ENMs can migrate via the bloodstream to different parts of the body. For example, it has been estimated that around 400,000 workers worldwide are affected by occupational exposure to nanomaterials in 2008 and the number will rise to 6 million in 2020 [63]. In terms of worker protection, there is thus a need to quantitatively assess and manage potential health risks, if possible [64].

ENMs can be used as powders, in dispersions or in a matrix and release primary particles. Products containing ENMs can be subjected to mechanical or chemical processes, such as spraying, washing, weathering, burning, etc., which can lead to the unintentional release of secondary ENMs, which can be inhaled, absorbed through the skin or via the gastrointestinal tract. Due to the exposure pathways, pulmonary, dermal and/or gastrointestinal exposure to nanomaterials may therefore occur.

Studies from 2000 onwards on e.g. nanoscale silver and silicon dioxide (nano-Ag, or SiO^2) have already stated that the greatest risk is posed by inhalation intake of ENMs [65][66][67]. A survey of nano-safety experts showed that 60% of respondents were concerned with inhalation exposure to ENMs – again reflecting the greatest safety concerns – followed by oral (30%) and dermal (20%) exposure [48]. Both inhalation uptake and deposition in the lungs are strongly dependent on particle size. Laboratory studies indicate that the dose-response relationship between nanoscale carbon black or titanium dioxide with toxic effects such as oxidative stress, inflammation or genotoxicity correlates with particle size [68][69].

In addition, other physicochemical and functional material parameters such as state of aggregation, density, surface properties, crystallinity, biological impurities as well as solubility rates and surface reactivity have toxicokinetic relevance [70]. Laboratory investigations using the example of pulmonary exposure in mice show that nanoscale titanium dioxide (nano-TiO2) has not caused any DNA damage compared to its larger counterparts, but has led to increased inflammatory reactions [71].

Reduced lung functionality and increased inflammation values were also found in workers exposed to nanoscale carbon black (carbon black) [72] In general, inhalation of ENMs is also associated with cardiovascular diseases, where not only the particle size but also shape has toxicological relevance. For example, inhalation of asbestos fiber-like ENMs, such as certain carbon nanotubes (CNTs), can lead to a malignant mesothelioma, the cause of which is related to the length, width and chemical composition of the fibers and their ability to remain in the lungs [65]. However, CNTs not only cause asthmatic inflammation [73], but several publications on bioassays in rats suggest that CNTs have carcinogenic effects as well [74][75]. These described health effects are not restricted to nanomaterials and can also be caused by non-nanomaterials but the nanospecific properties changes response, interaction, behaviour and toxicity and make risk assessment – if possible - more cost and time intensive [76].

3.1.2 Environmental Risks

As the described nano-safety research show, some nanomaterials can have negative effects on health and the environment, such as respirable asbestos-like particles and fibers. Although more recent studies rather address environmental interactions and transformation processes significantly influencing toxic effects (e.g.: particle agglomeration, dissolution), there is still a paucity of information and discrepancies in literature about their environmental impacts [74]. Thus, very little information is available about uptake mechanisms in living organisms and trophic transfer [52][77] as well as on specific toxicity [58], and it is very challenging to detect released nanomaterials in complex environments such as relevant technical compartments e.g. effluents, waste waters, and landfill leachates [78][79]. The expected future increase of environmental release and the consequent dissipative loss [80][81] demands not only a comprehensive analysis of nanospecific effects but an ongoing application of governance measures according to the precautionary principle.

Ecological research on the behaviour of ENPs can rely on numerous studies from the geo-sciences that have examined the behaviour of naturally occurring nanoparticles in the environment. Nonetheless, ENPs differ in certain respects from those occurring naturally. While natural nanoparticles are randomly structured and diffusely distributed in the environment, industrially produced suspensions or powders contain pure nanomaterials of very uniform size, shape and structure. Such nanomaterials have unique properties such as the high tensile strength of CNTs or the photocatalytic activity of nano-TiO2, which make them interesting for novel products and applications but also unpredictable when they enter the environment. Precisely these special features make it so difficult to predict the fate and behaviour of ENPs in the environment.

A short overview over the behaviour of nanoparticles in different environmental media, especially the fate of certain nanoparticles such as nano silver, titanium dioxide and carbon nanotubes is given below [82].

In the environment, nanomaterials can undergo a range of chemical processes that depend on many factors (e.g. pH value, salinity, concentration differences, the presence of organic or inorganic material). The characteristics and properties of a nanomaterial also play a major role. Bioavailability is decisive in determining potential toxicity. This depends strongly on whether nanoparticles remain stable in an environmental medium or are removed from the respective medium through agglomeration and deposition or are transformed into a form that organisms cannot take up.

Air: When nanoparticles enter the atmosphere, they move from zones of higher concentration to zones of lower concentration (diffusion). Air currents distribute the particles rap-idly; these can migrate great distances from their original source. Nonetheless, nanoparticles tend to aggregate into larger structures (agglomeration). Detecting nanoparticles in the air is very difficult because simple measurements of size distributions can hardly distinguish such agglomerates from natural particulates. The speed with which particles in the air are deposited on the ground, in the water or onto plants (deposition) depends on particle diameter. Nanoparticles from the air are deposited much slower than larger particles due to their smaller diameters.

Water: The general rule is that nanoparticles distributed in the water behave much like colloids, which are well described in the chemical literature. Colloids are droplets or particles that are finely distributed in a medium; they are relatively unstable because they rapidly adhere to one another due to electrostatic attractive forces and then sink as a result of gravity. Natural water bodies typically contain dissolved or distributed materials, including natural nanomaterials. As expected, synthetic nanomaterials that enter a natural water body bind themselves to such natural materials. The fate and behaviour of nanomaterials in the water, however, are also influenced by factors such as pH, salinity (ionic strength) and the presence of organic material. Naturally present organic material

(NOM) can lead to the decomposition of C60-fullerenes or of their aggregates and thus alter particle size and shape. A NOM such as humic acid can stabilize certain carbon nanotubes (MWCNT) in the water and thus prevent their settlement. Some CNTs are also deliberately produced through special surface changes so that they do not aggregate. The type of such functionalisation helps determine whether CNTs can be removed from a natural water body through sedimentation. As CNTs are very polymorphic, it is usually impossible to provide generally valid statements about their fate and behaviour in the environment. A strong influence of the surrounding environment on behaviour, in particular the presence of NOM, has also been determined for other nanomaterials such as metals or metal oxides [83].

Soil: Nanomaterials in the soil and in sediments are assumed to bind themselves to solids. The generally very low concentrations of particles in the groundwater support this notion. The bioavailability – and therefore the potential toxicity – of a nanomaterial for soil organisms apparently depend strongly on whether it binds to NOM. The bioavailability of nanosilver in complex media such as soil is considerably lower than in water because the reactive silver ions can bind to components in the soil (e.g. NOM) [84].

3.1.3 Nanowaste

A very important issue which turned up rather late both in public and in scientific discourse is the behaviour of nanomaterial-containing products at the end of their life cycle and their effects on waste streams and environmental media. This topic is insofar significant because it takes up a central recommendation of the European Commission to develop models and standards for risk assessment "throughout the whole life-cycle" of nanotechnological products. This discussion started in the member states alongside the discussion of overarching ideas connected to sustainable development, the application of safe-by-design principles and circular economy embedded in the political adaptation process of the sustainable development goal (SDG) debate.

Nanomaterials that enter the environment from diffuse sources can be classified as potential "nanopollutants" (for example titanium dioxide nano particles released from sunscreen lotions in surface waters) [85]. "Nanowaste" are materials that come into contact with solid wastes and can be collected separately. Titanium dioxide nanoparticles therefore become waste only when they are for example eliminated in wastewater treatment plants after the biological purification phase.

The behaviour of nanomaterials in waste incineration plants can be characterised as following: when incinerated nanomaterials can either be destroyed, converted into other nanomaterials (e.g. oxides, chlorides) or be released unchanged. Nanomaterials in the size class 100nm and larger are most efficiently removed in the filters of waste gas purification systems. Nanomaterials smaller than 100nm are only partially retained by filters. An estimated up to 20% can be released. Incinerating nanomaterials can accelerate the formation or destruction of undesired by-products (e.g. polycyclic aromatic hydrocarbons). Nanomaterials can be retained in the solid wastes (ash, slag, filter residues) produced by waste incineration plants. A leaching of nanomaterials from such wastes, for example when subsequently dumped in a landfill, should be avoided [86][87].

Various nanomaterials are currently incorporated in a wide range of products. It remains largely unknown whether these can pose an environmental or health risk when they end up in waste treatment plants or in landfills via various waste streams at the end of their life cycle. In a precautionary approach, several experts and organizations have therefore formulated first recommendations designed to minimize nanomaterials in wastes. Future research efforts should increasingly focus on the disposal phase of „nanoproducts" in order to better estimate potential risks. The possible environmental effects of nanomaterials and their fate in waste treatment has been a specific research topic in the Austrian nano-EHS-programme and an overview is given in several publications [88].

3.2 Scientific uncertainty

3.2.1 Complexity

According to the International Risk Governance Council (IRGC) complexity refers to the difficulty of identifying and quantifying causal links between a multitude of potential causal agents and specific observed effects in a system or a system component.[89] This may be valid to an extraordinary high level for nanotechnologies. First of all, nanotechnological substances and compounds can be formed from more than 50 different chemical elements, the most common being silicium, titanium, carbon and metal oxides. In the case of carbon the number of possible chemical compounds is almost unlimited. Only the C60-compunds are forming a vast field of research (Fullerenes and others) for which the Nobel prize has been awarded in 1996 to Smalley, Curl and Kroto. The next level consists of the physical behavior of nanomaterials in itself and their tendency to form aggregates and agglomerates on their own and with components of their environment. Nanomaterials can not only be described by their chemical behavior but also by their physical properties such as surface area, surface charge or catalytic activity. On the next level they will have to be described according to their behavior in natural environments (water, air, soil) and living beings, which adds to complexity the complexity of this environment. And finally, the universal applicability of nanomaterials in nearly every conceivable product and usage is to be considered.

The systematics of the EFSA risk assessment scheme might serve as an illustration for the complexity of nanomaterials, although in this case only the application field of food and food contact materials are brought to attention (see Figure 2) [90]. This guidance document provides an overview on information requirements and how to perform risk assessment of nanomaterials in the food and feed area (e.g. novel food, FCMs, food/feed additives and pesticides). The EFSA Guidance is aimed at providing a structured pathway for carrying out safety assessment of nanomaterials in the food and feed area. Under the EU Regulation on Novel Food (EU) No. 2015/2283, a food consisting of engineered nanomaterials will be considered a novel food and as such will require respective authorisation. The Regulation stipulates that risk assessment of novel foods shall be carried out by EFSA, which shall also be responsible for verifying that the most up-to-date test methods have been used to assess their safety. The risk of a nanomaterial is determined by its chemical composition, other physicochemical properties, its interactions with tissues, and potential exposure levels. The schematic general outline for risk assessment of nanomaterials is shown in Figure 5. Only to give an impression which information needs are considered by the EFSA to be necessary to sufficiently characterize nanomaterials, only the first step of physico-chemical characterization is listed here:

1. specific morphology (e.g. rigid, long tubes or fibres, high aspect ratio nanomaterials, fullerenes, crystal structure, porosity), carrier materials with cores and shells of different biopersistence (e.g. multifunctional nanomaterials);
2. complex transformations (e.g. ageing, changes in surface properties, porosity) or metabolites or de novo formed particles from ionic species
3. altered hydrophobicity/hydrophilicity;
4. persistence/high stability (e.g. in water, fat, or body fluids, lack of degradation/dissolution);
5. increased reactivity compared to equivalent non-nanomaterial (e.g. catalytic, chemical, biological);
6. targeted or controlled release by the nanomaterial;
7. nanomaterials having antimicrobial activity;

8 different or increased mobility of the nanomaterial in vivo compared to the conventional non-nanomaterial, i.e. possibility of increased bioavailability and internal exposure (e.g. transport via macrophages; transport through cell membranes, blood-brain barrier and/or placenta, delivery systems) and mobilisation potential (e.g. infiltration, sorption, complex formation);

9 interactions with biomolecules such as enzymes, DNA, receptors, potential 'Trojan horse' effects on immunotoxicity);

10 bioaccumulation;

11 quantum effects (e.g. altered optical, electronic, magnetic, mechanical or redox properties in nanoscale materials).

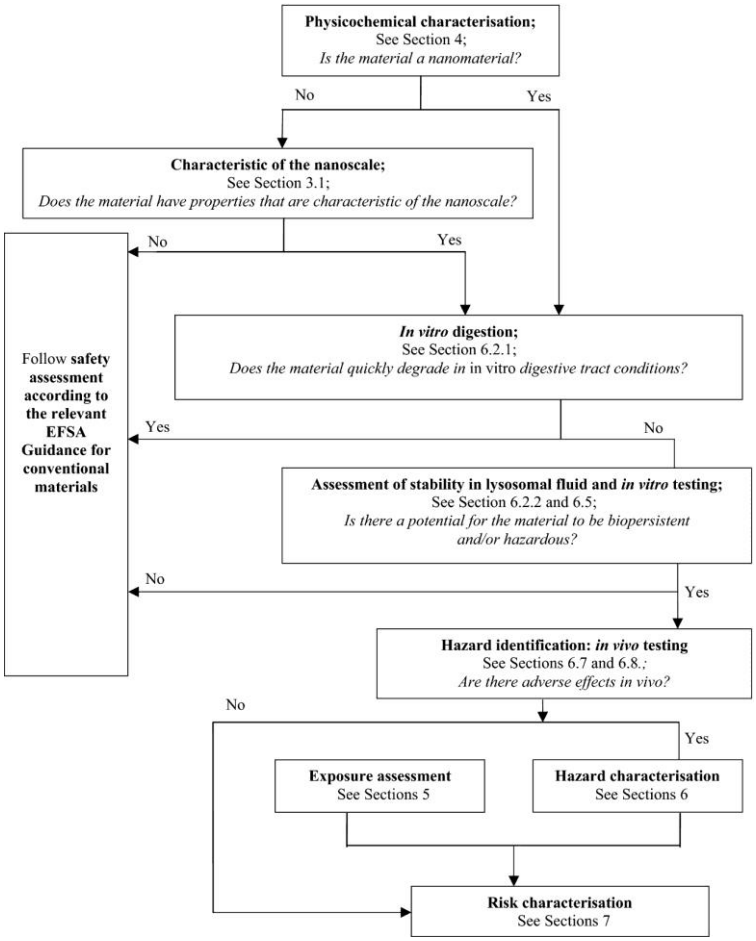

Figure 2 Example for complexity: EFSA schematic outline of risk assessment of ingested nanomaterials. [90]

3.2.2 Uncertainty

Silvio Funtowicz and Jerome Ravetz pointed out that in the context of technological systems and their impacts, human knowledge is always incomplete and selective and thus contingent on uncertain assumptions, assertions and predictions [91]. Because of their probabilistic nature this is valid for all scientific statements, but for emerging technological systems and new scientific developments this inherent uncertainty is absolutely decisive. Moreover, this contributes to their evolutionary flexibility. Regarding advanced materials

like engineered nanomaterials one has to add their general propensity to be used for a wide variability of applications. Therefore, talking of uncertainty additional sources of uncertainty have to be considered such as linguistic and terminological vagueness (this is the reason why terminology and metrology represent the first areas of standardisation – so too in nanotechnology). Additional aspects which might enlarge the uncertainties concerning new materials are the lack of data, the lack of measurement methods and protocols, inadequate measurement devices and generally the inability to ask the right research questions. Simultaneously the necessity to regulate the implementation of these new materials and products increases the pressure on decision-makers.

Seen in this light nanotechnology regulation has so far been rather the management of uncertainties than of risks and will for a long time stay like that. In the aftermath of the controversies surrounding genetically modified foods in the 1990s, nanotechnology faced calls for moratoriums and the need for a different approach to regulating new technologies with risks which cannot be fully characterized had become apparent [92]. This gave rise to self-regulatory cooperative approaches of actors in the field of nanotechnology, summarised under the term "nano governance", entailing a number of organised public and expert nano dialogues [93]. In Austria the nanosafety TA-project NanoTrust of the Institute of Technology-Assessment (ITA) at the Austrian Academy of Sciences (ÖAW) was an endeavour to foster such cooperative approaches. This project started in 2007 and is still in operation. It is described in detail in chapter 4.1.7 (risk management by network).

Technologies like nanotechnology and advanced materials are defined by uncertainties rather than risks. Governance processes of a technology characterized by a dominant risk frame will also be shaped by the availability of risk-relevant knowledge. While risks allow knowledge on possible outcomes and an expression in probabilities, uncertainty does not allow the assignment of probabilities to outcomes. Inter and trans-disciplinary deliberative expert dialogues can be a form of organising the process of knowledge creation and exchange when the prevalence of uncertainty is high [94].

An important contribution to identifying, structuring and evaluating the available information on a certain technology when it is in its infancy an independent and neutral actor is necessary to provide a platform of deliberation which is trusted by many if not all concerned parties. In the case of the Austrian nanotechnology debate this has been provided by the Austrian Academy and its project NanoTrust. Therefore, appropriate strategies to secure neutrality and independence are absolutely vital because of the threat to lose the necessary variety of potential aspects and the possibility to be instrumentalised by other, often funding organisations. In the case of NanoTrust the securing of independence and neutrality [94] has been achieved by several measures, such as

- Expanding the basis of support: while initially the project was funded exclusively by the BMVIT, it went on to include contributions of the Federal Ministry of Health (BMG), the Federal Ministry of Agriculture, Forestry, Environment and Water Management (BMLFUW), the Federal Ministry of Labour, Social Affairs and Consumer Protection (BMASK) and the Austrian Workers' Compensation Board (AUVA).
- Introducing an international advisory board, which convenes on an annual basis (twice annually during the first years) and is tasked with monitoring the strategic development of the project.
- Open and transparent communication: maintaining a culture in which it is possible to openly communicate is vital to ensure that the project tasks can be pursued appropriately, since it enables the project members to set boundaries for the NanoTrust work in a flexible manner, as is required when following a moving target. This necessitates the presence of trust between the funding bodies and project team. It is also important to communicate the exact roles of all involved people and also to clarify the functions to the network, allowing for transparency and accountability.

- Focus on a scientific basis: an example is provided by the NanoTrust dossiers, serving to disseminate fact-based information. The dossiers seek to summarize information on a specific topic in the area of nano-specific risks, primarily in the areas of health and environment.
- Official commitments and functions in official and federal committees and working groups, which on the one hand broadens the perspectives and options and on the other hand increases the perceived reliability of the participating project members.

3.2.3 Ambiguity

As the IRGC points out ambiguity includes two different aspects. Firstly, it denotes the variability of reasonable interpretations based on identical observations or assessments. This is the normal situation in research, especially in emerging fields which are on the brink of defining their research object. This type of ambiguity can only be solved by increasing research, generating data and fostering cognitive debate. The second aspect of ambiguity reaches far beyond the limited sphere of science and indicates situations where normative decisions have to be taken. In this case different appraisal of the same set of information is based on different values or world views.

The methodological debate following the seminal publication of Poland et al. [95] on CNT-toxicity in mice might serve as an appropriate example for scientific ambiguity. The authors found an increased propensity of mice to develop granuloma as consequence of chronic inflammation after inhalation (or rather instillation) of a certain type of carbon nanotubes. Whereas the authors insisted that their findings should be treated as preliminary result a lively debate developed focusing on issues like the application of different CNT tapes, the technical way of bringing the fibres into the mouse lung and even the applicability of the mouse model on human pathophysiological processes.

Scientifically ambiguous is also the way to define a dose which is one of the central questions on toxicology and still an unsolved question for nanomaterials because their effects are mainly based on surface properties and not on mass. In toxicology a dose can be either the mass/weight of a dissolved substance per volume (concentration/gram per litre) or the molar concentration of a dissolved amount of substance (number of atoms, to be calculated by the specific weight) per volume (molarity, mol per litre) or finally, the particle density or particle concentration per volume (particle counts per volume). The definition of dose depends very much on the circumstances the material in question will be produced, applied or handled.

However, even the concept of toxicology itself can be regarded as scientific ambiguous depending on the determining disciplinary background. The concept can be chemical-driven, morphology-driven or radiation-driven. In the case of nanomaterials, it has been suggested to apply the surface reactivity as the most important parameter. Up to now, the area and the surface reactivity have been considered the most important quantities in terms of dose. However, it is still unclear whether this understanding is actually accurate [96].

The last example illustrates decisional ambiguity and refers to the definition of threshold levels in workplaces where nanomaterials are used, manipulated and processed. Although there are still no binding workplace limit values for most fine dusts and dusts from nanomaterials, recommendations for significantly lower threshold values have already been proposed for some nano-substances. These recommendations vary depending on the responsible authorities even if they concern the same substances. For example, threshold levels for silica fine dust (SiO2) are recommended to be below 0.025mg/m^3 by the US National Institute for Occupational Safety and Health (NIOSH), while the European OSHA

(Occupational Safety and Health Administration) establishes 0.100 mg/m^3.[3] In Germany even lower values are valid since 2016. The threshold level recommended by German authorities lies at 50% of the OSHA value or 0.050 mg/m^3.[4]

Especially in the case of new and emerging technologies such as the nanotechnologies the occurring various uncertainties lead necessarily to a well-balanced application of the precautionary principle as long as the scientific evaluation is not fully clarified and reasonable assumptions of possible threats to human health and the environment exist.

3.3 Relevance of the PP to the case

The first mentioning of nanotechnology within an EU-level strategic document can be found in the 5th Research Framework Programme (FP5) of the European Commission (EC) for the period of 1998-2002 [12], articulating the priorities for the European Union's research, technological development and demonstration activities: *"In order to develop from a visionary perspective future and emerging technologies with a potential industrial impact, research topics could include, in a non-prescriptive way: [...] nano-scale, quantum, photonic, bio-electronic technologies, including future generation integrated circuits, ultrahigh performance computers and super-intelligent networks".*

Following a Communication regarding a European strategy for nanotechnology [15] stated: *"Despite some calls for a moratorium on nanotechnology research, the Commission is convinced that this would be severely counter-productive. Apart from denying society the possible benefits, it may lead to the constitution of "technological paradises", i.e. where research is carried out in zones without regulatory frameworks and is open to possible misuse. Our consequent inability to follow developments and intervene under such circumstances could lead to even worse consequences. The Precautionary Principle, as used up to now, could be applied in the event that realistic and serious risks are identified."*

The European Commission formulated a series of interconnected actions for the immediate implementation of a safe, integrated and responsible approach for nanoscience and nanotechnologies in 2005 [61] and adopted the Communication "Towards a European Strategy for Nanotechnology" mentioned here.

Within the action plan for Europe 2005-2009 for nanosciences and nanotechnologies, the European Commission reviewed relevant EU legislation to determine the applicability of existing regulations to the potential risks of nanomaterials. The Commission published a Communication in 2008 which stated that, despite the fact that the term "nanomaterials" is not specifically mentioned in EU legislation, the existing legislation covers the potential health, safety and environmental risks in relation to nanomaterials in principle [20] (see also chapter 2).

The EU Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR) and the Scientific Committee for Consumer Products (SCCP) identifies knowledge gaps and pointed out the need to improve the knowledge base, in particular regarding test methods and risk assessment (hazards and exposure) methods. *"An indication is given in the annexed Commission Staff Working Document Where the full extent of a risk is unknown,*

[3] U.S. OSHA: Standard No., 1926. 1153 -Respirable crystalline silica (March 2016),https://www.osha.gov/laws-regs/regulations/standardnumber/1926/1926.1153

[4] Nanoinformation.at, https://nanoinformation.at/fileadmin_nanoinformation/user_upload/Arbeitsplatzgrenzwerte_2019.pdf

but concerns are so high that risk management measures are considered necessary, as is currently the case for nanomaterials, measures must be based on the precautionary principle." [20] *"Measures adopted under the precautionary principle must be based on general principles of risk management and must therefore inter alia be proportionate, non-discriminatory, consistent, on an examination of benefits and costs of action or lack of action, and on an examination of scientific developments."* [13]

Nanotechnology opens up many opportunities and its fields of application are already numerous. However, human health and the environment must be protected - only in this way can the opportunities offered by the new technologies be exploited in the long term and in a sustainable manner. At the 11th Nano Authorities Dialogue in March 2017, which took place in Vienna, the representatives of the authorities of Austria, Luxembourg, Liechtenstein, Switzerland and Germany agreed on a catalogue of measures to promote the sustainable and safe development of nanotechnology. The "Vienna Declaration" was presented to the Council of the European Union (Environment) in June 2017.[5]

[5] https://nanoinformation.at/bereiche/regelungen/

4 Risk governance and the precautionary principle

4.1 Political and juridical dynamics

4.1.1 Legal acts

In this chapter, we focus on the political and juridical dynamics of nanomaterials with special emphasis on the EU and Austria. National legislation in the field of nanomaterials and chemicals regulation is highly dependent on EU-wide regulations. At European level, there are various pieces of legislation that regulate nanomaterials in e.g. consumer products, some of them in general and some of them in specific terms. These regulations are implemented in Austria, but also in the other member states of the European Union, within the framework of existing national legislation. Additionally, some of the Member States established national mandatory reporting systems for nanomaterials, which is addressed in chapter 4.1.2.

The first mention of nanotechnology within an EU-level strategic document can be found in the 5th Research Framework Programme (FP5) of the European Commission (EC) for the period of 1998-2002 [12], articulating the priorities for the European Union's research, technological development and demonstration activities: *"In order to develop from a visionary perspective future and emerging technologies with a potential industrial impact, research topics could include, in a non-prescriptive way: [...] nano-scale, quantum, photonic, bio-electronic technologies, including future generation integrated circuits, ultra-high performance computers and super-intelligent networks".*

Regulation of Chemicals: The instruments concerned with the legislation of nanomaterials in the European Union are the REACH Regulation (EC) No 1907/2006 (Registration, Evaluation, Authorisation and Restriction of Chemicals) [17], which has been in force since 2007, and Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of dangerous substances and mixtures [97], which entered into force in 2009. Nanomaterials are not explicitly mentioned but covered by the "substance" definition in both regulations, nor is the PP but *"REACH is based on the principle that manufacturers, importers and downstream users have to ensure that they manufacture, place on the market or use such substances that do not adversely affect human health or the environment. Its provisions are underpinned by the precautionary principle."* [98]. REACH requires companies that produce or import chemical substances in quantities equal or more than one ton per year to register these in a central database. Since 2009, the European Parliament has called for the introduction of a comprehensive scientifically based definition of nanomaterials in EU legislation, as well as a European nano-registry containing information on nanomaterials and their use on the European market. In 2011, the European Commission published a recommendation on the definition of "nanomaterial" [28], which was and still is not legally binding, but currently under review [99] but stated no need for a harmonized EU-wide registry. Since 2013, the European Commission has been examining to what extent REACH can be adapted to regulate nanomaterials and finally amended REACH Annexes in 2018, concerning new and already existing registrations and explicitly addresses nanoforms of substances. More specific requirements are thereby provided within the framework for the risk management of nanomaterials [100]. Nanoforms must be identified and characterised within the registration, whereby they can be documented individually or in joint sets of similar nanoforms. Information is to be provided on particle size, shape and surface properties of the nanoforms, as well as on volumes and uses of nanoforms.

Calls for a harmonised regulation on nanomaterials now go back a decade, referencing the unique aspects of nanotechnology [101]. Nevertheless, within the European Union the precautionary principle, as detailed in Article 191 of the Treaty on the Functioning of the

European Union [102], sets high standards regarding the health of humans and the environment, as well as consumer protection. This means that only products which have their safety tested may be placed on the market. Products containing nanomaterials are currently explicitly regulated within sector-specific legislation. To date, nanomaterials are specifically addressed within regulations for cosmetic products, novel foods, food contact materials, food additives, medical devices and biocidal products, including requirements for information on nanomaterials (labelling) and the safety assessment of these materials. In addition, there is a directive on disposal of electronic waste in which nanomaterials are mentioned [36]. The various sector-specific regulations are listed below and taken from our latest Dossier [103]:

Cosmetics: The Cosmetics Regulation (Regulation No 1223/2009) [23] stipulates that the European Commission is to be notified of the content of nanomaterials in cosmetic products. The content is to be declared in a list of ingredients by its chemical name followed by nano in brackets, e.g. "titanium dioxide (nano)".

The term nanomaterial is defined as *"an insoluble or bio-persistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm"*. The Cosmetics Regulation stated that all actions by the Commission and Member States relating to the protection of human health should be based on the precautionary principle.

Biocides: The Biocidal Products Regulation (Regulation No 528/2012) [33] requires specific assessment and approval of the nanoform. Nano silver, for example, must therefore be addressed specifically and does not fall under the assessment and approval of silver as such. Furthermore, the regulation requires the labelling of chemically active substances in nanoform.

The term nanomaterial is defined as *"a natural or manufactured active substance or non active substance containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm"*. The Regulation is underpinned by the precautionary principle to ensure that the manufacturing and making available on the market of active substances and biocidal products do not result in harmful effects on human or animal health or unacceptable effects on the environment.

Food and Feed: The Food Additive Regulation (Regulation No 1333/2008) [21] and the regulation on plastic materials and articles intended to come into contact with food (Regulation No 10/2011) [30] stipulate the specific assessment and approval of the nanoform of approved substances. In this regulation the PP is not explicitly mentioned.

Furthermore, the Novel Food Regulation (Regulation No 2015/2283) [41], comprising considerations in relation to specific requirements regarding nanomaterials: *"Novel foods should be safe and if their safety cannot be assessed and scientific uncertainty persists, the precautionary principle may be applied."*

The regulation on the provision of food information to consumers (Regulation No 1169/2011) stipulates that nanomaterials shall be clearly indicated in the list of ingredients. Regulation No 1169/2011 on the provision of food information to consumers defines engineered nanomaterials as *"any intentionally produced material that has one or more dimensions of the order of 100 nm or less or that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less, including structures, agglomerates or aggregates, which may have a size above the order of 100 nm but retain properties that are characteristic of the nanoscale".* The regulation does not explicitly mention the precautionary principle.

Medical devices: The Medical Devices Regulation (Regulation No 2017/7745) is also undergoing revision with serious reflection regarding the introduction of requirements for labelling and specific assessment of devices that contain nanomaterials.

The term nanomaterial is defined as *"a natural, incidental or manufactured material containing particles in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm; Fullerenes, graphene flakes and single-wall carbon nanotubes with one or more external dimensions below 1 nm shall also be deemed to be nanomaterials"*. The regulation does not explicitly mention the precautionary principle.

Electronics: The directive on restriction of certain hazardous substances in electrical and electronic equipment (RoHS Directive 2011/65) and the directive on disposal of electronic waste (WEEE Directive 2012/19) mention nanomaterials but have not introduced specific requirements.

The European Commission has, however, introduced the Observatory for Nanomaterials to provide information about existing nanomaterials on the EU market.

European Union Observatory for Nanomaterials: While there is no EU-wide nano-registry, the objective of increasing the transparency of nanomaterials on the EU market has prompted the establishment of the European Union Observatory for Nanomaterials (EUON), an online initiative funded by the EU Commission and maintained by the European Chemicals Agency (ECHA) since its formal kick-off in December 2016. The EUON gathers existing information but does not collect new data on the occurrence of nanomaterials and therefore cannot replace an EU-wide registry. The website began operation in the summer of 2017. The aim is to provide "reliable and neutral information" about nanomaterials available on the EU market. The website contains summary descriptions of product categories, uses, regulations as well as references to studies and reports, including details of existing national reporting systems. However, concrete data on individual products containing nanomaterials are missing.

4.1.2 National Nano-Registries

A quite different approach to regulate the production and use of nanomaterials and nanotechnologies is national mandatory registries. These registries, which have been established in several countries within the EU and the EEA (France, Denmark, Belgium, Sweden, Norway) operate in rather different ways (e.g. different trasholds and requirments). According to a current comparative analysis of EU/EEA Member States, Germany, The Netherlands and Italy have considered but not established a national registry so far [104]. The decision to not develop or implement nano-registries at this time can be related to concerns of creating trade barriers.

France: The French nano-registry "R-Nano" was issued in 2012 and has entered into force on 01. January 2013. It was the first European national registry for nanomaterials. The aim is to ensure the traceability of sectors using these substances, to improve the knowledge of the market and the volumes sold, and to obtain available information on toxicological and ecotoxicological characteristics.[105] Subject of the registration are artificially produced nanomaterials as defined by the European Commission, which are circulated in quantities of at least 100 g per year. Amongst the required information is the identity of the registrant, the substance identity, quantity, use and professional users. The "Agence nationale de sécurité sanitaire, de l'alimentation, de l'environnement et du travail" (ANSES) is responsible for managing the registry.

Belgium: The establishment of the Belgian nano-registry was decided by decree in 2014 and came into force on 01. January 2016. As of 01. January 2017, the registration of substances or mixtures produced in nanoparticle states (such as paints and sunscreens) is also obligatory. The registry is regulated by Royal Decree concerning the Placing on the Market of Substances produced in nanoparticle state from 27. May 2014.[106] The creation

of the registry is regarded as the first step in the management of nanomaterials and their impact on humans and the environment. The aim is to provide higher transparency about nanomaterials found on the market and about possible health risks. Traceability allows authorities to intervene, for instance in the case of a public health risk for workers. This registry is also intended to improve communication on nanomaterials for employees and in the commercial supply chain, with ambitions of strengthening public confidence in nanomaterials.

Denmark: On 13. April 2014, the regulation for a nano-registry was issued, which then came into force on 18. June 2014. The Danish nano-registry was introduced via Ministerial Order published in June 2014 (Danish Ministerial Order no. 644 from13/06/ 2014). Predating this, the Danish Chemicals Action Plan (2010-2013) already contained statements on nanomaterials and called for adjustments to REACH. The Danish Parliament consequently decided to establish an inventory of mixtures and products that contain or release nanomaterials (Danish Environmental Protection Agency Guideline for Danish Inventory of Nanoproducts).[107] The objective of the registry is to enable an overview of nano-products in Denmark and allow rapid intervention by authorities in the case of health risks.

Sweden. The Swedish Chemicals Agency (KEMI) published a proposal in 2013 where the mentioned the lack of a clear definition, inadequacy of REACH and CLP and need for a reporting system for nanomaterials. KEMI enshrined the registration of nanomaterials which entered into force on the 1st of January 2018 [108]. KEMI is also the responsible authority for the product registry. The first registration deadline was 28. February 2019 and so far there is no evaluation report available. The aim of the regulations is to create an overview of what nanomaterials are present on the Swedish market. The purpose is to gain information on the types and quantities of the nanomaterials used in Sweden [109].

Norway. Norway stated from the beginning that the existing EU legislation does not properly deal with nanomaterials and sympathised with the member state initiatives of mandatory registries. The duty to report to the Norway Product Register is determined by the "Regulations relating to the declaration of chemicals to the Product Register" [110] and information about the content of substances in nanoform must be provided, with the definition of "nanomaterials" following the EU Recommendation. The declaration of chemical products containing one or more substances in nanoform (mixture) to the Norwegian Product Register was obligatory from March 2015 and registration has to be done via an electronic declaration. The Product Register existing since 1981 is the official registry of hazardous chemicals in Norway and is managed by the Norwegian Environment Agency. The data of the registry is used to monitor chemicals, perform risk analyses related to chemical substances, compile statistics for the authorities, and to inform legislative work.

NanoTrust Dossier No.51en gives a concise overview over the recent developments regarding the use and the experiences with nanotechnology registries [103].

4.1.3 EU Code of Conduct

The Commission recommendation for a code of conduct for responsible nanosciences and nanotechnologies (N&N) research (code of conduct) dates from 2008 [24]. The code of conduct for responsible nanosciences and nanotechnologies research (code of conduct) is the Annex to the first nanotechnology-specific legal measure by the EU (2008), a Commission recommendation that is legally non-binding. The nanotechnologies code of conduct contains principles and guidelines for integrated, safe and responsible (ethical) nanosciences and nanotechnologies (N&N) research. The central control mechanisms are

research prioritisation, technology assessment, ethical and fundamental law clauses/restrictions, defensibility checks and accountability [111]. The core of the code comprises seven principles.

Principle of public well-being: Under the heading "Meaning", the Commission requires that N&N research should primarily serve the interest of the well-being of individuals and society and should respect fundamental rights (Paragraph 3.1) and that research funds should only be given to research that is useful to the general public. The code encourages research institutions and member states only to pursue research "with the broadest possible positive impact" (4.1.13) and in particular support research projects "aiming to protect the public and the environment, consumers or workers and aiming to reduce, refine or replace ani-mal experimentation" (4.1.13).

Principle of sustainability: Safe and ethical research should contribute to sustainable development (3.2); N&N research should not harm or create a biological, physical or moral threat to people, animals, plants or the environment. The code of conduct encourages the denial of funding to research that could involve a violation of fundamental rights or "fundamental ethical principles" (4.1.15), and human enhancement research (4.1.16). Finally, the Commission requires funding bodies to monitor the potential social, environmental and human health impacts of N&N research. (4.2.4).

Principle of precaution: N&N research should anticipate potential environmental health and safety impacts and maintain a high level of protection, avoiding risks without impeding in-novation (3.3, 4.1.5). As long as risk assessment studies on long-term safety are not available, nano-objects should not be intruded into the human body, food or other consumer related products (4.1.17). In order to protect workers and researchers against potential hazards and risks (4.2.1), the Commission insists on specific regulations and risk and ELSI re-search (4.2.5, 4.2.7).

Principle of democracy: The code of conduct envisions all stakeholders participating in the decision-making process (3.4, 4.1.8), research being conducted transparently (4.1.6)8, the presentation of research results being clear, balanced and comprehensible and made generally accessible (4.1.2, 4.1.4, 4.1.8, 3.1, 3.4). The EU is intended to serve as a forum for discussion to permit an appropriate debate on social concerns and hopes (4.1.1). The corresponding information and communication would be the responsibility of the Member States (4.1.1). All stakeholders are encouraged to participate in the determination of the content of N&N research (4.1.8, 4.1.10). Finally, the code requires the Member States and the research funding bodies to disseminate the code and its principles (4.3.1, 4.3.2).

Principle of excellence: N&N research should meet the best scientific standards (3.5), for which in particular the Member States and the research bodies are responsible. The Commission attempts to prevent "dubious practices" and to protect whistleblowers either through the employer or legal regulations (4.1.5). The code requires peers to verify the scientific results before they are widely disseminated (4.1.4).

Principle of innovation: N&N research should take place within an innovation-friendly environment (3.6), public authorities and standardising organisations should develop N&N research standards (4.1.11) and the Member States and research funding bodies should devote an appropriate part of research funds to risk assessment, standardisation and the refinement of metrology methods (4.1.12). The grant of funds should be preceded by a cost-benefits analysis (4.1.14) and funds should only be awarded if a risk assessment is presented together with the application for funding (4.2.3).

Principle of responsibility: Researchers and research organisations should "remain accountable for the social, environmental and human health impacts that their N&N research may impose on present and future generations" (3.7). To this purpose, researchers should conduct participatory foresight exercises (4.1.9). In order to ensure that the stakeholders actually comply with the principles of the code and other relevant

legal regulations, the Commission wants the Member States to provide sufficient resources to monitor and control N&N research (4.1.6, 4.3).

4.1.4 Nano-Standards

Another important approach to regulate the use of nanomaterials and nanotechnologies is standardisation. The Austrians standardisation committee 052.73 "Nanotechnology" consists of experts from research institutions, engineering and safety authorities. The committee is chaired by a member of the Institute of Technology Assessment (ITA) of the Austrian Academy. In 2019 a support project for AG 052.73 has been established at the ITA funded by the Austrian Ministry of Technology. The project is intended to generate additional knowledge on nano R&D, nano safety research and technology assessment and to increase the engagement of Austrian nano expertise in international standardisation projects, mainly the committees ISO/TC 229 "Nanotechnologies" and the CEN/TC 352 "Nanotechnologies".

The European CEN/TC is led by AFNOR, the French standardisation organisation (Association Française de Normalisation). Its scope is to increase the understanding and control of matter and processes at the nanoscale, typically, but not exclusively below 100 nanometres in one or more dimensions, where the onset of size dependent phenomena usually enables novel applications. Additionally, the technical committee strives to improve the utilisation of the properties of nanoscale materials that differ from the properties of individual atoms, molecules or bulk matter, to create improved materials, devices and systems that exploit these new properties. Specific tasks include developing standards for: classification, terminology and nomenclature; metrology and instrumentation, including specifications for reference materials; test methodologies; modelling and simulation; science-based health, safety and environmental practices; and nanotechnology products and processes. For the time being, 19 standards have been published since 2010, mainly on vocabulary (CEN ISO/TS 80004 series) and characterisation of nano-objects. Several specific guidelines have also been published in recent years, such as a guideline for Life Cycle Assessment (CEN/TS 17276:2018) and more recently guidelines for the management and disposal of waste from the manufacturing and processing of manufactured nano-objects (CEN/TS 17275:2018).

The technical committee at the International Standardization Organization (ISO/TC 229) is led by the British Standardisation Institute (BSI). The scope of the ISO/TC 229 is more or less congruent to the CEN/TC and focussed on a better understanding and control of matter and processes at the nanoscale and utilising the properties of nanoscale materials. The CEN/TC 229 has been founded in 2005 and 72 standards have been published up to now (April 2020), whereas 36 standards are currently under development.

4.2 Risk management

Risk management measures are dependent on the sector-specific pre-conditions and the concrete context where they are applied. An appropriate risk management regime will tremendously differ by scope, accountabilities and responsibilities. Because of the high variance of nanotechnologies and the fairly universal use of nanomaterials it is therefore not possible to give a one-for-all solution which can be applied to all applications and areas. In the following there have been two cases chosen to illustrate sector specific risk management activities, one case shows the reaction of the French government regarding the re-evaluation of titanium dioxide by the International Agency for Research on Cancer (IARC), and the other case certain management approaches concerning the handling of nanomaterials and nano-objects at workplaces. At least the risk management by networks is explained in the case of Austria.

4.2.1 Risk management by risk managers - Workplace safety

Worker protection and laboratory safety were very soon discussed as priority topics because the most exposed persons – those who are the first to come into contact with nanomaterials – are those involved in the production, transport and processing of these materials. Nanomaterials and products containing such materials are already in widespread use because they exhibit technologically interesting, nano-specific features such as increased tensile strength, improved electrical conductivity, special optical characteristics or special medico-chemical properties. But exactly these features (high reactivity) are also major risks for those persons who have to handle them.

As early as in 2007 several studies already reported data on exposure levels of nano-substances at the workplace[112][113]. In 2011, the German Council of Environmental Advisors also emphasizes, in connection with "precautionary strategies for nanomaterials", that one should concentrate "above all on a potential exposure at production and processing worksites"[114]. According to many of the worker safety relevant publications nanomaterials and nanosubstances create special challenges: Firstly, many of their characteristics – high reactivity and small particle size – make these materials technologically interesting, but also raise concerns because they could be associated with new health risks for employees. And secondly, the lack of robust monitoring systems for identifying nano-aerosols which could be inhaled makes it very difficult to determine contamination levels in the ambient and what measures can reduce such contamination [114].

Regulation on the international level: Internationally, a series of concise suggestions ('best practices') have been presented to deal with the risks at the workplace in the nanotechnology industry.[115][116][117] In 2013 resp. 2014 the European Commission published concise guidelines with detailed recommendations for handling nanomaterials both for workers and for employers [38][40].

Regulation at the national level: A "Guidelines for risk management in handling nanomaterials at the workplace" was commissioned by the Central Labor Inspectorate of the Austrian Ministry of Social Affairs in November 2010. It was designed to provide practically oriented and easily understandable support, especially for smaller and medium-sized businesses. This guideline orients itself according to traditional risk assessment methods for chemical agents. Beyond a list of recommended operational steps, it also contains a collection of summary-like descriptions (so-called theme sheets) on a total of 15 topics including definition and characterization, risk assessment, risk management, and measurement of nanomaterials [118]. In summer 2011, the Austrian Workers' Compensation Board (AUVA) published an official sheet "Nanotechnologies – Occupational and Health Safety" (M 310) designed to inform employees about protective measures for work-related exposure. The AUVA assumes that "the hierarchy of protective measures … is also [valid] for nanoparticles." Protective measures are to be established – as in other cases – based on a multi-level concept (substitution, technical, organizational and personal protective measures) [34].

There were also detailed recommendations published by scientific organisations (e.g. the US Research Council which focussed on laboratories) and industrial organisations (e.g. the German Chemical Industry Association or the Netherlands Federation of Chemical Industries). Together with the above mentioned governmental documents the recommendations arrive at more or less congruent statements, based on the precautionary principle (protective measures are to focus, as a precaution, on the suspected harmful features), hazard identification (safety efforts initially require recognizing potential threats although this is not always possible) and the application of cascading safety measurements (substitution, technical protection, organisational protection and personal care) [119].

4.2.2 Risk management by government - Ban of titanium dioxide in France

An example for a risk debate of nanomaterials and subsequent risk management is the case of titanium dioxide (TiO2). Already in 2006 the International Agency for Research on Cancer (IARC) of the WHO stated: „There is *inadequate evidence* in humans for the carcinogenicity of titanium dioxide", „There is *sufficient evidence* in experimental animals for the carcinogenicity of titanium dioxide", „Titanium dioxide is *possibly carcinogenic to humans (Group 2B)*" [120].

In 2017 an unexpected amount of nano-TiO_2 in food and cosmetic products was subject of public debate in France. Consumer protection groups first addressed that many cosmetic and food products do not fulfill the legal labeling requirements, having found them to contain nanomaterials without being labelled as such. The French General Directorate for Competition Policy, Consumer Affairs and Fraud Control (DGCCRF) confirmed the claims of the consumer protection groups [121], prompting a political response [122]. The debate surrounding TiO_2 (not solely nano-TiO_2) led to a petition to remove the food additive E171 (TiO_2) from the French market [121], with the French government ultimately deciding a ban on placing E171 and products containing E171 as a food additive on the market for at least the duration of the year 2020[6]. In 2019 the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) points to recent studies describing damage to intestinal cells and possible genotoxic damage related to E171 and emphasized the uncertainty surrounding the oral uptake of TiO_2 due to lacking data[7]. The European Food Safety Authority (EFSA) re-investigated the use of E171 as a food additive in light of the developments in France in 2019 and concluded that there is no new evidence to support a ban [123] . Concerning the risks of inhalation of TiO_2, however, the Committee for Risk Assessment (RAC) of the European Chemicals Agency (ECHA) has proposed in 2017 to classify TiO_2 as a category 2 carcinogen through inhalation under REACH regulation, following the ANSES' proposal of a classification as a class 1b carcinogen [124]. The debate surrounding TiO2 was mainly restricted to France and did not take place in German-speaking public arenas [125]. The example shows that the size-based definition narrows the view because investigations have shown that titanium dioxide is often used in sizes very close to 100 nm, so that it does not meet the definition and does not have to be labelled as a nanomaterial in food, for example. However, the properties of the particles just above the 100 nm limit do not differ significantly.

4.2.3 Risk management by network – Nano risk governance in Austria

The Austrian nanotechnology research programme (Nano Initiative - NI) started in 2003 and an accompanying technology assessment (TA) was suggested from the Institute of Risk Research (IRR) of the University of Vienna to complete the three existing R&D oriented research program lines [126]. Despite the recommendation of the NI it took more than three years to place the first safety-relevant projects. In 2006, the Institute of Technology

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[6] Legifrance (Rule No. 2018-938 vom 30. Oktober 2018) [LOI no 2018-938 du 30 octobre 2018 pour l'équilibre des relations commerciales dans le secteur Agricole et alimentaire et une alimentation saine, durable et accessible à tous]

https://www.legifrance.gouv.fr/eli/loi/2018/10/30/AGRX1736303L/jo/article_53

[7] ANSES (12. April 2019): ANSES Opinion No. 2019-SA-0036,

OPINION of the French Agency for Food, Environmental and Occupational Health & Safety

on the risks associated with ingestion of the food additive E171, 40 S.,

https://www.anses.fr/fr/system/files/ERCA2019SA0036EN.pdf

Assessment (ITA) at the Austrian Academy of Sciences has been assigned to produce a status report on the international environmental, health and safety (EHS) and ethical, legal and societal implications (ELSI) of research regarding nanotechnologies and nanomaterials by the Austrian Ministry of Traffic, Innovation and Technology (BMVIT) [127]. This may be interpreted as a strong indication for the fact that public debate on safety relevant issues have become more relevant to authorities by then [128]. In 2007 the NanoTrust project, dedicated to nano-safety and governance, was funded by the BMVIT.

In 2009, Austria addressed the central issues of nanotechnology by drawing up the Austrian Nanotechnology Action Plan (ÖNAP) [25], which was generated by the interdisciplinary cooperation of several federal ministries and agencies and institutions from science and economy, as a direct consequence of the ongoing discussion in the already existing nanotechnology network. The core of the Action Plan consists of about 50 recommendations for specific Austrian measures at national, European and international level and explicitly mentions the PP several times. The interdisciplinary working groups dealt with the topics 1) health and employee protection, 2) environment, 3) economy and 4) science, research and development. All interdisciplinary working groups invoke the PP. In all resumes it is implicitly mentioned.

Opportunities were seen primarily in the improvement of product properties. However, when considering nanomaterials in the work environment and worker protection, the focus is placed on the, as yet insufficiently clarified, possible risks to human health and the resulting uncertainties rather than the opportunities [25].

Nanotechnologies and products have the potential to make a significant contribution to resource and energy conservation as well as waste avoidance. When assessing the environmental impacts of nanotechnological processes and products, a life cycle-oriented approach is necessary [25]. To date, these considerations are often missing or incomplete. The results of the latest national project from the NanoEHS fund (NanoAdd) showed that industry (according to its own statements) tends to avoid the use of nanomaterials because of the high potential of uncertainty.

The Austrian Nanotechnology Action Plan states that nanotechnological innovations should strengthen Austria as an economic region. Resource conservation is a possible contribution to a more sustainable development of new products using nanomaterials, but this this has to be accompanied by in-depth risk research. Therefore, the national research funding program on environmental, health and safety of nanotechnologies (Nano-EHS) has been established in 2011 and is since then dedicated to foster research on safety aspects of nanomaterials.

A primary goal was to involve the public in the creation and implementation of the ÖNAP. Therefore, both the draft (2009) and the implementation report (2012) were subject to public consultation on the internet. The comments received were published and considered.

The beneficial aspect of nanotechnology seems to play an important role in terms of public acceptance as well as the safety of nanotechnological applications. The further development of safety research and regulation therefore occupies a major place in Austria and is also being pursued to date in the national NANO Environment, Health and Safety research programme and by the NanoTrust accompanying research project, which became a part of the Austrian nano risk governance landscape itself.

During the years since 2007 a complex system of different and complementary instruments to assess and to regulate the production and the use of nanomaterials has been established in Austria, engaging several dozen organizations and employing different formats and instruments such as a national communication strategy in nanotechnologies, a federal commission for nano safety and an independent nano safety research programme. The project NanoTrust has been involved in the conceptualization and practical implementation of these instruments from the very start in 2007. Figure 3 gives an overview over the main instruments of the Austrian nano governance system.

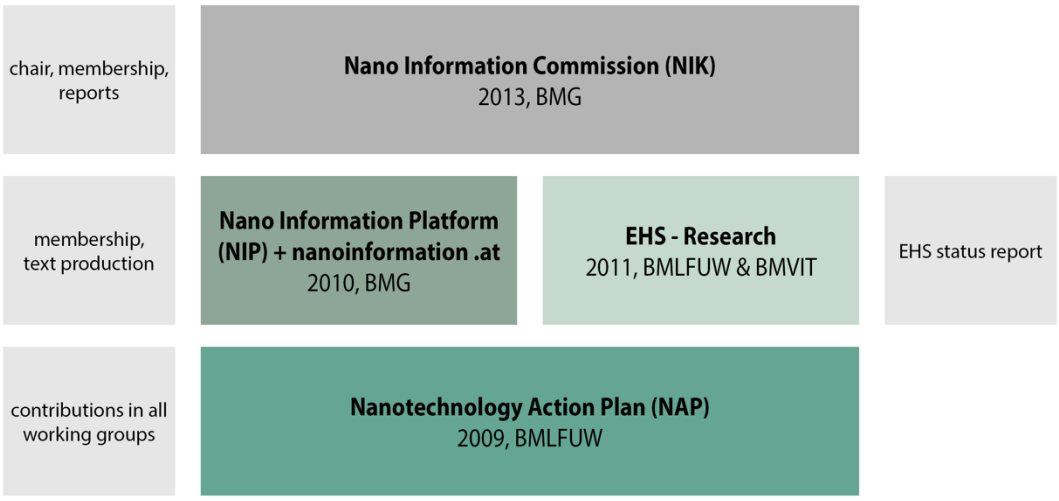

Figure 3 The Austrian nano governance system and the role of NanoTrust (grey fields) – *BMG … Ministry of Health, BMVIT … Ministry of Technology, BMLFUW … Ministry of Environment.*

The basis for the development and the core for the nano risk activities is the Austrian Action Plan Nanotechnology (NAP) published in 2010 which has been described earlier. A very important element regarding many of the conceptual aspects were drawn from the work of the long-term research project NanoTrust at the Austrian Academy of Sciences (s. above) which has since its inception in 2007 become an element of the governance system itself. NanoTrust has also played an important role in implementing and at least partly operating many of the main elements, it is involved in shaping the nano-EHS-research programme (and therefore not liable to apply for its scientific calls as a project partner) and serves as regular provider of scientific content regarding nano risk and safety issues for the public information portal nanoinformation.at.

One of the concrete outputs of the NAP was the foundation of a Nano Information Platform (NIP) aiming to bring together experts from a wide variety of fields to establish transparent public communication on the safe use of nanomaterials. The NIP is a non-formalised, open (people participate on a voluntary basis and they are free to come and go whenever they want) yet stable (as in the sense of committed people who participate from the onset) group of around 10 – 12 stakeholder representatives (ministries, safety agencies, NGOs and research organisations), coordinated by the Ministry of Health. NanoTrust has taken part in this public communication network from its very beginning in 2010 [126].

The result of these NIP expert discussions was the establishment of a nano-information portal (nanoinformation.at), hosted by the Austrian Ministry of Health yet being a common project of all the concerned ministries and other organisations such as the Austrian Academy of Sciences and Austrian Food Safety Agency. Since 2012, it ensures transparent public communication on the safe use of nanomaterials through a continuous information flow between experts and the interested public. It gives people the option to interact with regulatory authorities and experts in case there are questions and concerns. Consumers' questions are collected through the portal and answered within a 2-week timeframe after establishing an intercommunication process among collaborating experts. Material for this public information platform is developed in different self-organized working groups.

A stable working group on worker safety was established in June 2011, under the responsibility of the Austrian Worker Compensation Board "AUVA", the biggest insurance

company for workplaces in Austria. NanoTrust has initially suggested to install such a permanent working group and has since then been part of it and regularly takes part in their meetings until today. The nano – information portal establishes a two-way communication process by i) producing nano safety and risk relevant info addressing the interested public and ii) answering the consumers' questions. The NIP has been active since 2010, convening 2 or 3 times per year, being responsible up to date for the following tasks: operation and maintenance of the portal, public communication (consumers and the interested public), publication of risk and safety relevant documents produced by its members for use on the portal.

NanoTrust has been especially involved, from the onset, in the creation of the Nano Information Commission (NIK) of the Austrian Ministry of Health which represents the most formalised element of the Austrian nano risk governance landscape. The NIK was founded in 2013 as an advisory board to the Minister of Health. It consists of 23 members from ministries, agencies, universities as well as two NGOs. It convenes two to three times a year having as main tasks i) to provide all members with information on the current research and developments in the field of nanotechnology safety, ii) to offer an opportunity to discuss and evaluate these findings and iii) to foster safety-relevant research concerning the use of nanomaterials in Austria. The NIK is concerned with the implementation of the Austrian Nano Action Plan and represents the diversity of opinions and the professionally sound state-of-knowledge of various scientific experts. In contrast to the NIP, the NIK is not an open network: Proposals for new members can be made by the plenum. ITA designates one full membership and a substitute to the NIK. The chair is hosted for 5 years and currently held by the Coordinator of the NanoTrust project. In 2019 the Nano Information Commission started its second period of operation and the Coordinator of the NanoTrust project has been re-elected as chair until 2023.

4.3 Other governance dynamics

4.3.1 Public risk perception

Considering the public perception of risks with regard to technology controversies has increasingly become important since the debates on genetically modified organisms (GMOs) in Europe. The perception of risks by the population can differ tremendously from the expert judgement and in many cases does so. Risk Perception can be dissimilar in different cultures, societies, nationalities and between genders. Furthermore laymen (public), experts (risk community), policy makers, NGO´s and industry rate risks differently and hold different perspectives. Generally, laymen put more focus on severity of damage while experts place more emphasis on the probability of occurrence [129].

The topic of public perception of risks of nanotechnology has been studied institutions in the European region [130]. Table 1 shows a few studies on public risk perception carried out by European institutions.

Area	Title/Name of project	Authors/Publishing organisation	Time/Period	Methodology
EU 27	Eurobarometer 73.1: Biotechnology	TNS Opinion & Social (Brussels) on behalf of the European Commission	2010	Quantitative

Area	Title/Name of project	Authors/Publishing organisation	Time/Period	Methodology
GER, CH	Nanotechnology from the perspective of consumers	Eidgenössisches Department des Inneren (EDI), Bundesamt für Gesundheit (BAG), Stiftung Risikodialog	2012	103 qualitative individual interviews
GER	Nanoview	Bundesinstitut für Risikobewertung (BfR)	2013	Quantitative

Table 1 European risk perception studies. [130]

The European Commission regularly monitor the publics opinion on various topics. In Eurobarometer 55.2: Science and Technology in the Awareness of Europeans, nanotechnology per se was first mentioned as relevant technological future developments but the topic was met with little interest in 2001 (compared, for example, with medicine). It also revealed that the population, in their own estimation, said they had very little understanding of the technology itself [131]. In 2005s Eurobarometer 63.1: Europeans, Science and Technology the topic nanotechnology was still of little interest with 8% compared to medicine with 61% [132].

The European Eurobarometer of 2010, under the topic of "biotechnology", was inter alia concerned with nanotechnologies as one of several investigated "new" technologies. More than 26.600 personal interviews were carried out in all 27 EU member states, on a representative scale according to the respective populations. The study showed that the topic of nanotechnology was largely unknown to the population. Nanotechnology was generally significantly less known than genetic engineering, however, with large differences with regard to nationality, gender, level of education and level of information among the questioned persons.

The assessments of nanotechnology and consequences were quite unspecific. Some questions and statements were met with clear positions by the test persons: For example, they agreed that nanotechnology was "unnatural", but also that it was "good for the national economy". They quite clearly rejected that "nanotechnology makes you uneasy". With regard to other questions, the responses were less clear and more evenly distributed among "Agree", "Disagree" and "Don't know" (e.g. with regard to nanotechnology helping people in developing countries, being safe for future generations, benefitting some peoples but putting others at a risk or constituting a harm to the environment). The majority viewed nanotechnology as good for the economy, but there were large country differences (20%-60%), whereby the level of knowledge plays a decisive role.

The study "Nanotechnology from the perspective of consumers" was conducted in 2010 in cooperation between the Swiss Federal Department of Home Affairs (Eidgenössisches Department des Innern, EDI), the Swiss Federal Office of Public Health (Bundesamt für Gesundheit, BAG) and the Risk Dialogue Foundation (Stiftung Risiko-Dialog). The study analysed 103 qualitative, open and personally conducted interviews in Baden-Württemberg (53) and in German-speaking Switzerland (50). The same contained a care-fully selected and near-representative selection of tests person with regard to gender, age and level of education [133]. The study confirmed the above generally low level of awareness of nanotechnology. Knowledge on specific fields of application and possible usage decreases with the exception of cancer treatments, paints/polishes, textiles and cleaning agents.

Generally, while the population does not have a clearly more negative attitude than earlier, the topic's ambivalence has increased (49%), ambivalence has increased (49%), including the expectance of risks (67% expect health risks, 40% expect environmental risks). Overall, nanotechnology does not play a role in their perception (40%). The study also addresses the question of social trust: With regard to actors, science and authorities enjoy the largest trust.

The German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR) conducted inter alia a study on the public opinion of nanotechnology in the project "Nanoview" and on possible communication strategies [37]. This study analysed a representative sample of the German population, consisting of 1200 persons. 200 of these test persons received detailed information on nanotechnology in advance in order to determine the influence of information material on risk perception. The study shows – similar to the Eurobarometer – that the unawareness of nanotechnology as well as its assessment as increasingly important. While the test persons are more critical in their weighing of risks and benefits than in an earlier study in 2008, the majority of the population still remains positive. The acceptance of nanotechnology depends on its field of application: Application distant from the body, as well as environmental and medicinal application generally are seen more positive. With regard to social factors, the most important variables of the study are gender and age: Men tend to be better informed and more positive than women, young people better than older people. Education, house-hold size, income or migration background were not found to have an influence on the attitude of the test persons.

All in all, it can be observed that with regard to the German speaking area (Germany, Austria, Switzerland) (studies ranging from 2006 to 2013) found that the topic of "nanotechnology" was largely unknown to the population with a low level of risk perception and a low level of awareness of nanotechnology. A well-established standard of high level of precautionary regulation can be seen as a positive effect on the public risk perception in this case and area [130].

4.3.2 Public dialogue

Nanotechnology has been massively influenced by dialogue.[8] The spectrum ranges from stakeholder dialogues to participatory dialogues and even to informational sessions that are now often described as dialogues. Governments also call for and promote dialogue as the political instrument par excellence for the responsible use of nanotechnology. The German federal government, according to its 2015 Plan of Action, therefore wants to conduct "a comprehensive dialogue with the public about the opportunities and effects of nanotechnology" [134]. Moreover, if one considers that the Synthetic Nanomaterials Action Plan adopted by the Swiss government views "communication and promotion of open dialogue about the opportunities and risks of nanotechnology" as the first and most important measure to be taken,[135] and that the Austrian Nano-Action Plan takes "developing cooperation and reinforcing the dialogue and transparency among all stakeholders, including the general public" to be a central task [25]. Public dialogue obviously has a political dimension and has become a political reality in the context of the management and regulation of new technologies, both on the transnational and national levels [136].

[8] For a collection of dialogue projects on nanotechnology, see the European Commission webpage under http://ec.europa.eu/research/industrial_technologies/policy-dialogues_en.html

The action plan on nanotechnology of the European Commission as well as numerous national action plans (e.g., Austria, Germany and Switzerland) suggest activities especially in two areas in order to achieve responsible risk management. Firstly, it seeks to intensify research on environmental and health risks (EHS), and secondly, it encourages the establishment of scientifically founded risk communication processes in order to contribute to an informed public debate [137].

Dialogue processes constitute the method of choice for risk communication activities. They enable the creation of a connection between societal actors, especially politics, the public, industry and academia and establish a platform for the institutionalised and focused exchange between the communication participants. Those dialogues can be informational, consultative or participatory. During the years every type of dialogue process has been employed on various aspects concerning the production and use of nanotechnologies and nanomaterials. Table 2 gives an overview over the most important nanotechnology dialogue processes carried out in the German speaking countries.

Type	Germany	Austria	Switzerland
Information meeting	nanoTruck	NanoInformationsPortal	Expo Nanotechnologies
Participatory dialogue	NanoSafety-focus groups	NanoSafety-focus groups	publifocus
Consultative or stakeholder dialogue	NanoDialog of the NanoKomission	Nanotechnologie-Informations-Plattform	BAG NANO-Dialogplattform

Table 2 Dialogue processes in German speaking countries. [137]

Political and scientific discussions on nanotechnology focused on the concern that the public or finally the consumers could respond to the newly implemented key technology with similar fears concerning risks and thus with rejection as it already was the case with some subareas of biotechnology and genetic engineering (e.g. green genetic engineering, cloning) [2].

In Switzerland, the population was surveyed using the publifocus method in 2006, which is a dialogue procedure developed by TA-SWISS. This allows an early contribution to an objective discussion of the possible consequences of technological progress. This method is not used to draw up recommendations and the results do not claim to be representative of Switzerland as a whole. However, they do reflect the population's assessment and provide concrete indications of further fields of action. Results show that there were societal concerns about ubiquitous communication technology, both ethical and social, as privacy and human rights could be threatened by nano-sensor networks, computers and microscopically small nano-cameras and nano-microphones, which could enormously increase surveillance. There were also concerns about the use of nanoscale instruments in medical diagnostic like nano-implants [138].

4.3.3 Media coverage

Media have a significant influence on the public image of science and technology, especially in areas where the public usually has no direct contact with and no immediate idea about the research field. The media play an important role in the formation of society's opinion by drawing attention to selected topics and bringing them closer to the public. This has been specifically the case for nanotechnologies. Especially in the beginning of the public discussion on nanotechnologies quality press such as the "Neue Züricher Zeitung" (Switzerland), the "Frankfurter Allgemeine Zeitung" (Germany) and "Der Standard" (Austria) introduced to central aspects of technical applications, which also include the opportunities and risks associated with the new technologies. A comprehensive media analysis study for the German speaking countries has been conducted during the cooperative project NanoPol[9], details of on the method and the results of this media analysis were published elsewhere [139].

Various actors are usually consulted by the media on their evaluation of the possible opportunities (chances) and threats (risks) of nanotechnologies. Scientists are the group of actors who are by far most frequently mentioned. This is typical for science reporting, as is the fact that the majority of the articles appeared in the science sections of the newspapers. Around 20% of the actors are persons from the field of business, a result confirmed by the strong thematic interest in commercially relevant fields of application. According to the above-mentioned study political actors played a comparatively small role, with neither political institutions nor decision-makers making a significant contribution to the media discourse on nanotechnology. This is due the fact that nanotechnology has mainly been treated as scientific topic and not as a political topic. Civil society organisations such as environment or consumer protection organisations, which tend to adopt a rather critical approach to controversial technical developments and mostly take-up opposing positions to the actors from science and business, also appeared in a rather reluctant role, at least in the German speaking media.

The reporting on nanotechnology in the media in the three German-speaking countries is largely science-centred and attracts a generally low level of attention amongst the broad public thanks to its less emphasised placing. Finally, a focus on risks and controversial reporting, a concern raised regularly in expert circles, was not observed in the media. Risk topics played a role in fewer than 20 % of articles, whereas the benefits and opportunities of nanotechnology, on the other hand, were mentioned in 80 % of all articles. Benefits are seen above all for science [140].

[9] The "NanoPol" project was a cooperation between the Institute for Technology Assessment and Systems Analysis (ITAS) at the Karlsruhe Institute for Technology (KIT), the Institute for Technology Assessment (ITA) at the Austrian Academy of Sciences (OeAW), TA-Swiss in Berne and the Programme for Science Research of the University of Basel which lasted from 2010 to 2014. Several results of this cooperation were published in Gazsó, A. & Haslinger, J, 2014, Nano Risiko Governance. Der gesellschaftliche Umgang mit Nanotechnologien, Springer, Berlin

5 The precautionary principle and its future

5.1 Innovation principle

Nanotechnologies (in the beginning mentioned together with nanosciences) have been advertised as a promising new field of technology from the beginning. Future foresight experts stated that "the next big thing is really small"[141] and tried to convince interested parties to invest in innovative solutions in practically all conceivable areas of concern, starting from material physics, over new construction material, paints and varnishes, water and dirt repelling surfaces to new diagnostics and efficient drug delivery systems.

The European Commission set its hope in nanotechnologies and nanosciences in its action plan of 2005 and promotes nanotechnology as an area which will have highly promising prospects for turning fundamental research into successful innovations. But innovation is expected not only as mere art but in close connection to safety and sustainability. The Commission emphasises its will not only to boost the competitiveness of the European industry but also to create new products that will make positive changes in the lives of the European citizens, be it in medicine, environment, electronics or any other field. In the foreword to the action plan the then science commissioner Janez Potocnik mentions such applications as new engineered surfaces for better performance, new medical treatments for fatal diseases such as brain tumors or Alzheimers' disease, and new supercomputers using nanoscale components.

On the national level the innovative potential of these new group of materials has been always tightly linked to safety considerations. The German Research Strategy of 2007 lays its emphasis on the safe use of nanomaterials on workplaces and therefore seeks to foster research in the fields of human and environmental toxicology. Main goals should be the identification of nanomaterials, their chemical reactivity and their effects on living systems. Most important questions to answer are the possible exposition of persons on workplaces and the potential exposition of consumers. A necessary prerequisite for an effective risk management would be the adaptation of proper detection and measurement systems [142].

The recent updating of the common research strategy of the German authorities makes this tight interconnection between innovation and safety again clear: A safe and environmentally compatible design of innovative materials and their secondary products should largely rule out unacceptable risks for people and the environment right from the start. This can be achieved by either using inherently safe materials (safety of application) or a product design that is low in emissions and environmentally friendly over the entire life cycle (integrated application safety). Moreover, the consumer has to be properly informed and supported in applying these innovative materials and their products. Research priority 2 of the new research strategy aims at supporting the research institutions and industrial producers in developing application-safe and environmentally compatible material innovations and their use in secondary products by applying proper design processes (safe-by-design, see below) [143].

However, nanotechnological scientific discoveries do not generally change society directly but they can set the stage for change in a context of evolving economic needs. Nanotechnology is so diverse and complex that its effects will take time to work through the socio-economic systems [144].

5.2 Effect of the PP on innovation pathways

The innovation principle can be regarded as the counterpart to the precautionary principle which should be regarded in regulatory decisions whenever precautionary legislation is under consideration [145]. Critics warn of the risk that the innovation principle, whose origins lie in the industrial sector, could undermine the precautionary principle and make it easier to circumvent EU safety requirements [146]. The juxtaposition of safety and innovation reflects a rather fundamental misunderstanding of the concept of safety which often is regarded as simple absence of risk which eventually means the absence of action. Safety is nothing of all that. Apart from the eminent influence of empirical data on the development of safe machinery and working processes, safety and sustainability have innovative aspects in themselves and considering safety aspects often lead to new and rather unexpected solutions. Therefore, integrating safety aspects in an early stage of technology development can be regarded as fostering innovation rather than hindering it.

For this reason, nanotechnology research has been accompanied by safety and sustainability research from the beginning. Unfortunately, the recent research policy tends again to favour strictly disciplinary research and limits the space for activities which seeks to employ genuine interdisciplinary research and development of new technologies. The main goal is the integration of safety aspects in innovation processes as early as possible.

In the case of nanotechnologies, the concepts of green engineering resp. green chemistry (as "green nanotechnology") and safe-by-design have been thoroughly discussed and are still under scrutiny. Projects like NANoREG, NANoREG2 and ProSafe even contain separate work packages for elaborating the concept of safe-by-design.

Green nanotechnology. United States Environmental Protection Agency (EPA) drew up the "Green Chemistry Framework", whose aim is to achieve a reduction of the production and use of hazardous substances. These principles were modified to be applied on the development of safe nanomaterials. NanoTrust lists a total of 12 Green Chemistry principles, which inter alia require real-time monitoring of synthesis processes or the development of chemicals and products that are degradable and do not accumulate in the environment [147]. The German Nano Commission lists the following green nano principles to ensure the safe and sustainable development of nanotechnologies and introduces the term "benign by design": [148]

1) Biomimetics

- Use of local materials and energy sources as well as renewable resources
- Use of molecular self-organization as a manufacturing paradigm (e.g. biomineralisation for the manufacture of hierarchically structured, anisotropic, self-healing substances)
- Physiological manufacturing conditions (e.g. aqueous synthesis)

12 Resource efficiency

- Atomic efficiency and molecular specificity (e.g. through preventing side reactions, use of enzymatic reactions, precision manufacturing, miniaturization/dematerialization, elimination of cleaning process, and avoidance of rare materials etc.)
- Energy efficiency (e.g. improving production efficiency (electricity generation, light), reducing process temperatures, lightweight construction etc.)
- Recyclability (e.g. avoiding losses through using limited range of materials, segregation/modular waste collection, minimizing use of additives and processing aids, avoiding diffuse emissions and contamination of materials)

13 Minimum risk – benign by design

- Avoidance of toxic substances and nanostructures or morphologies which pose a risk to health or safety or to the environment
- Avoidance of problematic structures, morphologies and hazardous substances (e.g. bioaccumulation, persistence, ability to cross cell membranes)
- Responsible use of nanofunctionalities (e.g. preference of nanofunctionalities with less risks to human health and safety or to the environment or substitution of hazardous substances by inter alia selection of material and form, coating etc.)
- Prevention and minimization of potential exposure (e.g. through avoidance of mobility, bioavailability, being bound through a matrix or containment during process)

14 Energy and environmental technologies

- Emissions reduction
- Environmental monitoring
- Environmental remediation in and ex situ
- Switch to renewable materials and energy sources

Safe-by-design (SbD). There are a number of concepts that use design approaches to aim for increased safety and hence can be qualified as SbD concepts, as well as those that include elements of SbD. All of them address the reduction of risks by including safety-relevant considerations in the innovation processes as early as possible and taking account of the entire life cycle of the material or product [149]. In recent years, many national and international projects have been dedicated to the SbD concept per se and to its practical implementation in industry. Alongside the strengths of the concept, such as the early addressing of safety-relevant issues, currently, however, a number of challenges concerning practical applicability have been identified. On EU level several projects like NANoREG, its follower NANoREG 2 and others have taken up the topic of SbD or focused on the earliest possible inclusion of safety in the innovation process for nanomaterials, products and processes. Table gives an overview of relevant research projects which include the elaboration of the SbD-concept.

Project title	Funding programme
NANoREG	FP7
NANoREG 2	Horizon 2020
ProSafe	Horizon 2020
NanoGenTools	Horizon 2020
NanoMile	FP7
NanoFase	Horizon 2020
EC4SafeNano	Horizon 2020

Project title	Funding programme
caLIBRAte	Horizon 2020

Table 3 EU projects on Safe-by-Design and the early integration of safety in innovation processes. [149]

5.3 Reflection on the PP in the literature

The Precautionary Principle has been the basis for many regulatory decisions regarding the development and implementation of nanotechnologies during the last 15 years. Even the establishment of a regulatory system as complex as the Austrian nano governance system can be interpreted as guided by precautionary considerations. As a consequence, it is reasonable to assume that all continuing concepts such as RRI which are elaborating the PP will play a considerable role in managing emerging risks in connection with new and advanced materials, nanomaterials being one important group of them.

Concepts such as the EU's Responsible Research and Innovation (RRI) shows that societal values and aspirations should be integrated stronger at the political level into the innovation process. Schomberg (2013) provides a (preliminary) definition of RRI: "Responsible Research and Innovation is a transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) acceptability, sustainability and societal desirability of the innovation process and its marketable products"[150].

On the EU level projects like Nano2All and GoNano try to fathom the relevance of the guiding principles of RRI. The European research project GoNano focuses on the public engagement dimension of RRI, especially on the aspect of co-creation of knowledge and products. It tries to unite industrial demands and public expectations applying various participatory approaches. The GoNano project analyses the framework of responsible research and innovation and its applicability for the development of emerging technologies, especially nanotechnologies, according to the four main dimensions of responsible innovation: anticipation, reflexivity, inclusion and responsiveness[10].

[10] http://gonano-project.eu/about-gonano/

6 Synthesis

The term nanotechnology has been introduced by several reports by the US National Science at the end of the 1990ies. As a new field of scientific interest nanotechnology research has been announced to serve as universal solution to many technical and non-technical problems, especially in various sectors of industrial production, but also in pharmaceutics and medicine. Because of their high variability and universal use nanotechnologies are considered to be key enabling technologies (KET). Together with other scientific and engineering approaches such as biotechnologies they belong to a cluster called converging technologies because of their high potential to be combined with other organic and inorganic matter on a small scale.

In the case of the extraordinary diverse field of nanotechnology, it became apparent very quickly that risk and safety issues were not or at least not sufficiently addressed under the existing regulatory regimes (food safety, workplace safety, chemical regulation) and the existing approaches to hazard identification, evaluation and risk management. Therefore, traditional exposure and risk assessment (including e.g. modelling or testing approaches) were not applicable for nanomaterials and risks for human health and/or the environment could not be ruled out.

From an early onset the European Commission propagated an "integrated and responsible approach" on nanotechnology in its Nanoscience and Nanotechnology Action Plan of 2005 based on the precautionary principle. Simultaneously, it strives to integrate innovation and sustainability (safety being one important aspect of sustainable development) by requiring the provision of favourable conditions for industrial innovation on the one hand and the respect ethical principles, integrate societal considerations into the R&D process at an early stage. Several national nanotechnology action plans were to follow this outline, such as Germany (2006), Switzerland (2008) and Austria (2010). All of these political approaches to develop nanotechnologies in a safe and responsible way were based mainly on three cornerstones, i.e. the advancement of an independent nanotechnology risk research, the establishment of a transparent public communication strategy on nanotechnologies and the support of national and international network building on risk and safety issues regarding the development and use of nanomaterials and nanotechnologies.

Toxicological research took up issues of human and animal health and environmental integrity regarding the fate of nanomaterials in living beings, their organs, cells and environmental media such as air, water and soil. Environmental, health and safety research (EHS) has been intensified several times during the past European and member state nanotechnology research programmes. Specific risk assessment schemes, such the ones of EFSA or ECHA, show the complexity of the topic and emphasize the uncertainties and ambiguities of the available knowledge. The enormous need of specific data makes it necessary to connect the many research programmes and specific national nanosafety projects of on to each other and in multi-level databases.

Regarding the regulatory situation at European level, there are various pieces of legislation that regulate nanomaterials in consumer products (cosmetics, novel foods, biocides, food contact materials), some of them in general and some of them in specific terms. These regulations are implemented in the member states of the European Union, within the framework of existing national legislation.

These juridical documents and directives are complemented by a multitude of pre-legal and quasi-legal provisions, such as standards, registries, guidelines and codes of conduct. Nanotechnology registries for example have been established in several countries within the EU and the EEA (France, Denmark, Belgium, Sweden, Norway) and operate in rather different ways. Another important approach to regulate the use of nanomaterials and nanotechnologies is standardisation. Nanotechnology standards are developed in international committees such as ISO/TC 229 "Nanotechnologies" and the CEN/TC 352 "Nanotechnologies" since more than 10 years. They are actively supported on the national

level by the national standardisation authorities such as DIN (Germany), BSI (UK), AFNOR (France) or ASI (Austria).

At the same time risk management procedures have been developed to effectively regulate the use of nanomaterials and nanotechnological procedures at national and international level. Many of these efforts have been increasingly linked to each other to exchange practical and procedural experiences, e.g. the "Behördendialog" of the German speaking countries and the nano risk governance system of the Austrian Nanotechnology Action Plan and its executing elements such as NanoTrust, the Nano Information Commission and the Nano Information Platform. Because of the high variance of nanotechnologies and the fairly universal use of nanomaterials it is not possible to give a one-for-all solution which can be applied to all applications and areas. To develop effective risk management measures, they have to be tailored to the concrete context where they have to be taken. An appropriate risk management regime will therefore tremendously differ by scope, accountabilities and responsibilities. Main emphasis has been laid upon workplace safety and consumer protection at a very early stage.

Considering the public perception of risks with regard to technology controversies has increasingly become important since the debates on genetically modified organisms (GMOs) in Europe. Keen not to live through the same mistakes which have been made in earlier cases nanotechnology research policy cared for public risk perception and participatory inclusion of consumer concerns from the start of the research programmes. This has been accompanied by the establishment of more or less open and transparent information policies, at least from side of the national and international authorities. Nanotechnology has been massively influenced by dialogue. The spectrum ranges from stakeholder dialogues to participatory dialogues and even to informational sessions that are now often described as dialogues.

The European commission and consequently many of the member states have made the attempt to integrate the allegedly opposing concepts of innovation and safety in the case of nanotechnology research and development. Unsurprisingly, already the European Nanotechnology Action Plan contains both provisions for fostering innovative technology development and the integration of health and safety issues to a comparable degree. In the case of nanotechnologies, the concepts of green engineering resp. green chemistry (as "green nanotechnology") and safe-by-design have been thoroughly discussed and are still part of on-going research projects. Upcoming activities are ready to make use of the guiding principles of RRI and the Sustainable Development Goals (SDG), especially the application of new and advanced materials and technologies for managing complex global challenges.

7 Conclusion

Technologies like nanotechnology and advanced materials are defined by uncertainties rather than risks. Governance processes of a technology characterized by a dominant risk frame will also be shaped by the availability of risk-relevant knowledge. While risks allow knowledge on possible outcomes and an expression in probabilities, uncertainty does not allow the assignment of probabilities to outcomes. Moreover, several aspects of emerging phenomena are influencing the available knowledge on a specific technology. Lack of data and/or measuring procedures contribute to statistical uncertainties, the formation of new borders of the research field lead to terminological and linguistic vagueness, and new results of various and very different research projects are object of cognitive discourse and ambiguous interpretation.

For all these reasons an appropriate regulation of emerging technologies is not that much risk management than the management of uncertainty depending both on the quality of the available information and of the willingness of people with very diverging interests and motives to co-operate. Inter and trans-disciplinary deliberative expert dialogues can be a form of organising the process of knowledge creation and exchange when the prevalence of uncertainty is high. On the other hand, the integration of different interest groups and their values and concerns can contribute information that might be decisive for choosing an appropriate development path of a new technology. Finally, responsible authorities will have to take decisions on risk and safety relevant issues such as consumer protection, workplace safety and product liability which cannot be fully based on scientific understanding. This means that regulatory decisions have to be secured by additional aspects such as responsibility, accountability and social benefit.

Science, especially Technology Assessment, is able to make an important contribution to identifying, structuring and evaluating the available information on a certain technology when it is in its infancy. An independent and neutral actor is necessary to provide a platform of deliberation which is trusted by many if not all concerned parties. In the case of the nanotechnology debate during the last decade scientific actors have been central organisers of inter- and transdisciplinary risk and uncertainty assessment procedures. In Austria this has been provided by the Austrian Academy of Sciences and its long-term research project NanoTrust which started in 2007 and is still active. Therefore, appropriate strategies to secure neutrality and independence are absolutely vital because of the threat to lose the necessary variety of potential aspects and the possibility to be instrumentalised by other, often funding organisations. In the case of NanoTrust the securing of independence and neutrality has been achieved by several measures, such as expanding the basis of support: while initially the project was funded exclusively by the BMVIT, it went on to include contributions of the Federal Ministry of Health (BMG), the Federal Ministry of Agriculture, Forestry, Environment and Water Management (BMLFUW), the Federal Ministry of Labour, Social Affairs and Consumer Protection (BMASK) and the Austrian Workers' Compensation Board (AUVA).

An additional aspect which contributes to the stabilisation of risk and certainty assessment procedures is the building of national and international networks, either by establishing high level advisory boards or by forming specific working groups and committees. The involvement in the pragmatic work of international standardisation authorities (like CEN and ISO) and organisations (like OECD) increases the visibility of national expertise and contributes to the continuity of workflow and social integration.

An open and transparent communication maintains a culture in which it is possible to openly communicate is vital to ensure that one can pursue given tasks appropriately. This necessitates the presence of trust between the funding bodies and scientific assessment procedures. It is also important to communicate the exact roles and functions to the network, allowing for transparency and accountability.

Science based political counselling regarding the development and regulation of nanotechnologies demonstrated the importance to focus on a scientific basis. An example is provided by the NanoTrust dossiers, publicly available information material which is meant to serve as baseline for taking qualified decisions. The dossiers seek to summarize information on a specific topic in the area of nano-specific risks, primarily in the areas of health and environment and will be read by political decision-makers, funding organisations, safety personnel and experts from responsible governmental organisations like ministries and agencies.

Eventually, the appropriate management of emerging technologies like nanotechnologies and their uncertainties is essentially dependent on inter- and transdisciplinary co-operation and co-production of resilient knowledge. This requires both confidence in governmental and societal regulatory processes and trust in the people who are responsible for organising and maintaining these processes. Only by the willingness of these people to contribute to a common goal, in this case the safe and responsible development of nanotechnologies, and the good-will to assume the same willingness in everybody concerned, ensures the necessary stability and continuity that is the basis for building safe systems. The development of innovative technologies which make also sense in a societal way is certainly not a short-term project and requires the support of any substantial expertise as nanotechnology risk governance systems have shown. Long-term projects like NanoTrust can help draw attention to the specific lessons we have learned by this new approach of integrating innovation and safety at an early stage in technology development.

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