NanoDialogue of the German Government

ExpertDialogue 6.1

# Opportunities and risks of active materials at the nano scale

Documentation

Institut für Ökologie und Politik GmbH

Authors: Antonia Reihlen, Bernd Giese, Dirk Jepsen

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ÖKOPOL GmbH Institut für Ökologie und Politik

Nernstweg 32–34 D – 22765 Hamburg

www.oekopol.de info@oekopol.de

Tel.: ++ 49-40-39 100 2 0 Fax: ++ 49-40-39 100 2 33

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### **1** Introduction

The German Government's NanoDialogue on the opportunities and risks of nanotechnologies has been taking place since 2006 and is led by the Federal Ministry for the Environment, Nature Conservation, Nuclear Safety and Consumer Protection (BMUV). Since 2011, the dialogue has taken place in the form of 2-day ExpertDialogues with a focus on specific topics.

The ExpertDialogue on opportunities and risks of active materials at the nano scale was postponed by almost two years due to the Corona pandemic and took place with 23 participants to guarantee the minimum distances in the conference room. Unlike in the previous ExpertDialogues, the industry sector unfortunately did not participate in this one.

The aim of the dialogue was to obtain an overview of the substances or building blocks constituting active, nanoscale materials as well as the typical structures and functions of active, nanoscale materials. The examples of application and potential uses presented at the Dialogue made it possible to discuss the opportunities and risks in concrete terms and clarified the state of research and development. Presentations on the challenges of regulation as well as ethical thoughts on the use of (active) nanomaterials completed the perspective on the topic.

This documentation is a summary of the content of the presentations and the subsequent discussions, including explanations, which were given in response to questions. This summary does not attempt to reproduce the enormous scientific depth of detail of the presentations. The focus is rather on the main aspects regarding the benefits and risks of these materials. In the last chapter, core aspects of the ExpertDialogue are summarised from the moderator's point of view. This summary is not a conclusion that was agreed with all participants.



## 2 Introduction and overview: What are active materials at the nano scale?

Dr Bernd Giese, Institute of Safety/Security and Risk Sciences, University of Natural Resources and Life Sciences (BOKU), Vienna

Bernd Giese first presented the research field of active, nanoscale materials on the basis of a bibliometric analysis of scientific publications. Since the beginning of the 2000s, the terms "active" and "nano<sup>\*"1</sup> have been found with significantly increasing frequency in publications. Among the many disciplines involved in research and development of active, nanoscale materials, chemistry and materials science are particularly important. Biochemistry and molecular biology are also among the top 10 disciplines. A network analysis of the keywords used in the scientific publications showed that, with regard to the functionalities, chemical reactions (e.g., radical formation, enzymatic reactions), sensory activities (above all through plasmon resonance), energy storage and luminous effects are particularly important. In addition to metals, transition metals and carbon structures such as graphene, synthetic polymers and biopolymers such as nucleic acids or proteins are used for the production of active, nanoscale materials.

Mr Giese then addressed the question of differentiating active, nanoscale materials from passive nanomaterials and first presented a classification by Roco<sup>2</sup>, according to which nanostructures are differentiated into generations: The second generation of active nanostructures shows a change in behaviour or structure during the application compared to the first, passive generation.

A later classification according to Tour<sup>3</sup> attributes an "elaborate function" to active nanomaterials in contrast to passive ones.

In a more recent study by ECHA<sup>4</sup> it is proposed to distinguish active from passive nano structures based on the state of thermodynamic equilibrium: Passive materials are in a metastable thermodynamic equilibrium, while (re-)active ones are in a non-equilibrium state and can absorb and convert energy from their environment.

<sup>&</sup>lt;sup>1</sup> The asterisk means that the search also covered compound terms where "nano" is only the first part of the word, such as "nanomaterial".

<sup>&</sup>lt;sup>2</sup> Roco, M.C. (2004) Nanoscale Science and Engineering: Unifying and Transforming Tools. AIChE Journal, Vol. 50, No. 5

<sup>&</sup>lt;sup>3</sup> Tour, J. (2007). Nanotechnology: The Passive, Active and Hybrid Sides. Gauging the Investment Landscape from the Technology Perspective. Nanotechnology Law and Business, 361-373.

<sup>&</sup>lt;sup>4</sup> Camboni et al. (2019) A State of Play Study of the market for so-called "Next Generation" Nanomaterials. European Chemicals Agency, Ref.-No. ECHA-2019-R-14-EN, ISBN: 978-92-9020-726-9, DOI: 10.2823/242422

The energy involved can take various forms, for example:

- Chemical energy, e.g. catalytic functions, molecular processors in information processing, photodynamic therapy
- Electrical energy, e.g. electrical properties of carbon wires, graphene and Ag<sub>2</sub>O for transistors, semiconductors for energy storage
- Radiant energy, e.g. quantum dots for imaging, plasmon resonance
- Mechanical energy, e.g. in nanomotors driven by chemical, acoustic or magnetical effects, shape-changing three-dimensional RNA and DNA structures.

In the ECHA study, market research was carried out and a total of 47 applications of active, nanoscale materials were identified. It was found that the medical field predominates in this collection (drug delivery, imaging and theranostics). Other focal points are around sensor technology as well as electronic and electrical components and devices (displays, RFID tags, rechargeable batteries, etc.).

Only 8 applications were assigned to a third generation of "multifunctional nanosystems" in the ECHA study. However, the identified technologies of this more complex level were mostly still in the research phase. The focus here is also on medical applications. Other uses would be data storage or processing.

In the presentation, it was pointed out that active, nanoscale materials, the use as socalled "nanocarriers" for (targeted) drug delivery is an important field of application, especially in pharmacology. Active carrier structures are being developed for the spatially and temporally targeted release of an active substance. Complex products develop in this field, which even have genes for the blueprint of the active ingredient as well as a synthesis apparatus, show an increasing similarity to living cells.

Mr Giese concluded with the observation that, as predicted by Roco, the nano-, bio-, information- and cognitive sciences are converging recognisably - albeit to a still very limited extent - and an increasing integration of the different approaches in the materials produced is becoming apparent. Little information is currently available on the emissions of active, nanoscale materials from their application systems and the possible exposure of humans and the environment. However, it is foreseeable that certain applications outside closed systems may also be associated with releases over the life cycle of the materials.

#### Discussion

There was discussion about whether the differentiation of active and passive nanoscale materials on the basis of thermodynamic equilibrium is purposeful. Compared to earlier definitions, the reference to the physical units of energy and work was considered more objective. However, it was criticised that the dissolution of



materials (in water) already represented a borderline case that could be interpreted as "activity" according to the definition. In addition, the term "active, (nanoscale) materials" is not familiar in science. In the medical field, such a separation would not make much sense since many transformations take place at the interface to biological systems.

It was noted that the applicability of a definition depends on its purpose and that there is currently no legislative need for a clear-cut definition.

However, the thermodynamic perspective on active, nanoscale materials was also seen as a way to facilitate risk assessment. If an active, nanoscale material were to "completely react" and thus be reduced to a passive material, the risks of (also) this form could be assessed.

### 3 Active, nanoscale materials in medical applications

## 3.1 Active materials at the nano scale in medicines – nano meets bio

#### Prof. Dr Aigner, University of Leipzig

Mr Aigner introduced how various interactions (have to be) taken into account when developing active, nanoscale materials for medical applications. Using nanocarriers as an example, he showed that the interplay of the carrier's properties with the active ingredient is crucial for the efficiency and speed of release. Since the carrier interacts with biological structures, the distribution, uptake and processing of the active ingredient can also be influenced by them. The biological environment can change nanocarriers, e.g. by forming an outer layer (so-called "corona") or by breaking down the carrier. Nanocarriers can be modified so that (external) stimuli, such as the pH value or ultrasound, can be used to enable the targeted release of active substances.

Nanocarriers have been used in medicine for a very long time and can consist of many different substances. The use of active, nanoscale materials for drug delivery in medicine has various benefits:

- Active substances can be transported more efficiently to their sites of action and "activated" there in a targeted manner.
- Active substances can be used that are not usable without carriers because, for example, they are too unstable (in the body) or poorly water-soluble or (especially in the case of highly water-soluble) cannot pass through cell membranes.

- Combinations of active ingredients can be packed into a carrier and simultaneously transported to a site of action in the optimal mixing ratio.
- Side effects can be reduced by using smaller amounts and, depending on the specificity of the carrier, non-target tissue can also be protected from the active substance (up to targeted delivery).

According to research to date and since a risk-benefit assessment is carried out in the approval of pharmaceuticals, it is currently assumed, according to Mr Aigner, that the benefits of nanocarriers outweigh the risks in many cases. Depending on the composition of the carriers, there is good tolerability, e.g. with naturally occurring or easily excreted nanocarrier components. However, not all theoretically possible concepts of nanocarriers are also suitable for application, since, with increased complexity, difficulties in development or production (e.g. in upscaling) and in approval are to be expected.

Mr Aigner concluded his presentation by showing various research activities for the development of novel tumour drugs. He also showed research on active substances based on small RNA molecules (siRNA). These can inactivate genes at the level of expression, i.e. before the corresponding protein is formed. siRNA-based drugs are thus very efficient and have a lot of potential, but because of their strong negative charge, their size and their instability in organisms, they depend on carriers.

#### Discussion

In response to a question, Mr Aigner explained that the more complex the molecules are, the more difficult it often is to apply (new) nanocarriers in pharmaceuticals. This is due, among other things, to the fact that the manufacturing processes are more complex and thus less reproducible and controllable – "simple systems" are therefore preferred in the market.

One question related to how "targeted delivery" works. Mr Aigner explained that the nanocarriers do not "actively" move to the site of action but are distributed in the body with the blood. However, due to the specific binding sites of the carriers, they are "held" at their target cells and the active substance accumulates there. In leukaemia treatment, active substances could thus reach the target cells particularly efficiently and can be absorbed by them. In other cases, however, the efficiency of the drug delivery is significantly lower.

With regard to cancer research and the example presented, Mr Aigner clarified that with the "packaged" siRNA, initially only a slowing of tumour growth could be achieved. However, it must also be taken into account that the "repackaged" active substances or the new active substances that can only be used with the carriers are compared with therapies in which different active substances and procedures are



combined. Therefore, corresponding comparisons of efficacy are not very meaningful. It would also be possible to combine the new active substances with the other, established therapeutics and thus arrive at better therapies.

### 3.2 Active materials in pharmacology

Prof. Dr Andreas Herrmann, DWI RWTH Aachen

Mr Herrmann complemented Mr Aigner's presentation with examples of four functionalities that can be enabled with active, nanoscale materials as carriers in pharmacology. He emphasised that DNA and RNA molecules are often used as scaffold materials because they can create different superstructures, are easy to produce and can be easily linked with other substances and materials. Basically, due to the way the materials' properties are taken advantage of, the production of the desired structures would be self-organised.

For nanocarriers, Mr Herrmann showed that not only is a containment of the active ingredient possible, but it can also be bound "externally" to nanostructures. For antibiotic eye drops, functionalised DNA structures with lipids would be used, which bind to the surface of the eye and thus prevent the active ingredient from being washed out of the eye quickly. With this technology, both the concentration of the active ingredient in the eye drops and the frequency of application could be greatly reduced, which would result in better acceptance by patients and a reduction in side effects. In addition, studies with immunostimulants formulated with nanoparticles showed that a stronger immune response can be triggered due to their improved passage through cell membranes. One possible application would be in immune-based cancer treatment.

According to Mr Herrmann, active, nanoscale materials can also be used to produce active substances, such as antibiotics, in a more targeted manner. In experiments, areas of a (active) substance molecule to be modified were shielded with the help of a cage-like nucleic acid structure and thus protected from unwanted reactions during the necessary synthesis steps. Other molecule regions that were to be chemically modified remained free and could react. This could make the synthesis of active substances much more efficient.

Mr Herrmann went on to show that active, nanoscale materials can be specifically activated with external stimuli. For example, active substances packaged with DNA strands could be activated with ultrasound by splitting the DNA strands through the shear forces generated by the sound waves and thus releasing the active substances. Activation with the help of ultrasound would have the advantage over the already known activation with the help of light ("optogenetics") of a greater penetration depth into body tissue.

A final area of research into active, nanoscale materials is a time dependency in the release of active substances in the body. According to Mr Herrmann, cellular, enzymatic degradation processes are used here, among other things, which lead to a time delay in the release of the active ingredient.

For all examples of possible uses in pharmacology, the functionality is only achievable through the superstructure of the active, nanoscale materials.

#### Discussion

In the discussion, questions were asked about the use of DNA as a "building material", among other things regarding its stability against enzymatic degradation. Mr Herrmann answered that DNA is a good carrier material because it organises itself three-dimensionally and forms structures without forming covalent bonds. In addition, DNA could be stabilised by chemical modifications and would be degraded to endogenous substances, which is why it can be assumed that no damage is to be expected.

### 3.3 Sensors at the nanoscale for optical diagnostics

Prof. Dr Wolfgang Fritzsche, Leibniz-Institute of Photonic Technology in Jena

Mr Fritzsche explained the possibilities of using active, nanoscale materials in optical diagnostics.

Conventional optical diagnostic methods use fluorescent markers that indicate whether a "receptor molecule" has bound a target molecule, e.g. whether a certain pathogen has been detected in a sample or not.

In the presented method "Localised Surface Plasmon Resonance" (LSPR) gold nanoparticles are used. The measuring principle is based on the fact that the position and thus the colour of the resonance generated by oscillating free electrons changes depending on the type, size and shape of the particles used as well as on the ambient conditions. For this purpose, the surface of the gold particles is equipped with a receptor in the form of a DNA single strand whose sequence is complementary to the DNA being searched for (e.g. the DNA of a pathogen). If a DNA binds to this receptor, the colour of the light emitted by the gold nanoparticle changes in comparison to the "unloaded" particle. This colour change can be measured.

The gold particle sensors are fixed and can be regenerated by detaching the target molecules. In a microarray, sensors for different target molecules can be used and evaluated. Mr Fritzsche named the following advantages of this technology compared to conventional methods:



- The method enables detection of molecules without the need of labelling, i.e. no marker molecules need to be bound to the sensor DNA or the DNA to be analysed in an additional step.
- High sensitivity: Even a few bonds are sufficient to detect the presence of a target molecule.
- Efficient and cost-effective: As several sensors can be used simultaneously, the sample material can be amplified in a single suitable polymerase chain reaction (PCR).
- The evaluation can be carried out comparatively quickly and thus meets the requirements of short-term analyses, such as the search for the causative agent of sepsis.

A disadvantage of the method is that the evaluation has to be done in the laboratory, so it is not possible to "directly read out" the results.

#### Discussion

In response to a question, Mr Fritzsche explained that gold particles, which do not bind target molecules, act as controls because they emit the light of the original wavelength in the test system. As a rule, most sensors in an array retain their basic colour.

In the discussion, it was clarified that a DNA-based analysis is always preceded by a PCR, since the DNA to be detected must be amplified (and cleaved). This step determines the speed and is also necessary with conventional methods. The advantage of LSPR is that a mixture of different DNAs can be amplified in only one PCR and then measured directly - i.e. multiplexing is possible, in which a large number (<100) of different analyses can be carried out with only one PCR.

Regarding the possible applications, Mr Fritzsche explained that although at present mainly DNA was being worked with, other molecules could also be detected. This is also the subject of current research.

## 4 Quantum Dots - a new class of materials for display technologies

#### Dr Armin Wedel, Fraunhofer Institute for Applied Polymer Research

Mr Wedel reported that the trends in display technology were moving towards more flexible, interactive and wearable displays, as well as towards more brilliant colours and increased resolution. In addition, ways to simplify display manufacturing and reduce costs are being worked on.

Mr Wedel explained that currently mainly inorganic semiconductor materials are used as quantum dots (QDs) in displays. QDs are between 1 and 10 nm in size and are characterised by their chemical composition, band gap, size, surface, and shape, among other things. Different elements would be used, e.g. silicone and germanium, as well as compounds, e.g. cadmium selenide or indium phosphide. Cadmium compounds are increasingly being replaced by other compounds because of the restrictions in the Directive on Restrictions of Hazardous Substances in Electric and Electronic Equipment. <sup>5</sup>

QDs emit light of a specific wavelength when electrons return to "their" valence band after optical or electrical excitation. The wavelength of the emitted light (light colour) can be adjusted by the particle size. The size distribution of the QDs determines the emission width (width of the emission spectrum) and the QDs' surface influences their brightness.

Mr Wedel explained that one of the ways QDs are produced is as a "one-pot synthesis". The particles grow continuously and when the synthesis is stopped, particles of a certain size, and thus a colour, can be taken out. In further synthesis steps, the so-obtained core particles can be stabilised by adding polymers, for example. In this way, it is possible to produce all the required colours with just one type of material.

Advantages of using this type of QDs are, according to Mr Wedel:

- A homogeneous particle size distribution can be achieved and thus a very narrow-band emission can be obtained that almost approaches the emission width of lasers.
- One material can produce all visible colours except for pure blue and can also radiate in the IR range.

<sup>&</sup>lt;sup>5</sup> Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment



- The production can take place in solution and the QD surface can be well functionalised.
- QDs are very insensitive to heat, oxygen, light and water.

QDs can improve existing products and processes or enable entirely new technologies. Examples of applications are: fluorescent markers in diagnostics or spectroscopy, infrared displays and infrared markers, emitter material in QDLEDs (quantum dot light-emitting diodes) or QD lasers, semiconductor layers in transistors or absorber materials in photovoltaics.

Mr Wedel presented current research in which hybrid QDLEDs are being developed. Here, the QDs act as an emitter layer and are combined with organic materials. The advantages of these hybrid LEDs are a very high efficiency and the fact that the QDs can be synthesised from one material (see above). The aim of this research is to develop QDs that do not require indium, cadmium, or selenium.

#### Discussion

Some participants asked whether it can be safe to handle some of the semiconductor materials that also have toxic properties, including in the waste phase. Mr Wedel recalled that these materials are encapsulated in the respective devices and layers, and therefore release is almost impossible. However, emissions could occur in the waste phase.

It was critically noted that indium is a very rare raw material whose availability is estimated at about 15 years. It was foreseeable that its use would become impossible in the medium term and that it would therefore be necessary to recover it from waste. It could not be clarified at the ExpertDialogue whether it is possible to recover semiconductors from displays in old products.

## 5 Nanomaterial based electronic noses – curse or blessing?

#### Dr Martin Sommer, KIT Institute of Microstructure Technology

In his presentation, Mr Sommer explained how an electronic nose works and showed possible applications. Basically, electronic noses are modelled on the human nose and could replace complex, gas chromatographic measurements in certain applications.

According to Mr Sommer, an electronic nose developed at the KIT contains a total of 16 sensors that work together and simultaneously. The sensitive material of the

individual sensors is tin dioxide, which changes its electrical resistance depending on the gases present. All sensors of the electronic nose react differently to the gases present so that the 16 individual signals result in characteristic signal patterns for individual odours.

For an electronic nose to recognise an odour, it must first learn it. This is done by frequent exposure of the receptors to the corresponding odour. In the process, patterns from the signals of the receptors are stored for the different gas mixtures - and used as a reference for the respective odour. Depending on the planned use, the electronic noses are exposed to relevant odours. In the application, new odours are then identified by comparing the similarity of their patterns with the stored patterns of the previously learned odours.

Possible applications of electronic noses are: diagnosis of diseases based on the smell of bacteria (e.g. periodontosis), freshness control of food, search for drugs and explosives, mine detection, fire detectors (registration of smouldering and recognition of the materials, differentiation of cigarette smoke and fire), final control of industrial products that should always have the same smell or the control of water quality. The electronic nose is already on the market and in use as a fire detector in battery charging boxes, e.g. for e-bikes.

To get clear results, the electronic nose can also be combined with other measurements, e.g. humidity and temperature.

The concrete benefit of the electronic nose lies in a fast and cost-effective analysis of certain facts. Mr Sommer named challenges in the protection of personal data as a possible social risk, since very personal information, e.g. about a person's state of health, can be obtained from smells.

#### Discussion

In the discussion, it was explained that the electronic nose is made of only one material, is inexpensive to produce and can be used universally. However, each nose has to "learn" individually. There is no universal reference for odour patterns that can be used.

Some speakers pointed out that nanofibres can be a health concern because (short, rigid) fibres can physically damage the lungs. Longer fibres can also be problematic because they can break down into shorter, more harmful fibres. It was added that the tungsten oxide in nanoform - used alternatively besides tin dioxide - is considered genotoxic. In the measurements of the toxicity of tin dioxide, it should be considered that it was determined in oral studies and the bioavailability is low; there are no data



for inhalation exposure so far. However, the amount of nanofibres used in the electronic nose was stated to be very small and the fibres to be so firmly attached to the surface of the electronic nose that the risk of the fibres detaching is also considered very low.

In response to a question, Mr Sommer explained that the electronic noses can be cleaned by evaporation. Only in the case of heavy deposits on the sensors, e.g. from grease or dust, could the electronic noses only be cleaned at great expense or even be damaged. However, the presence of several sub-sensors in an eNose ensures a certain redundancy and thus robustness against the failure of individual sub-sensors.

## 6 Nano-sensors in lightweight construction and highperformance materials

#### Prof. Robert Böhm, HTWK Leipzig

In his presentation, Mr Böhm first introduced the COST Action, a European cooperation in science and technology that promotes various activities. The network EsSENce<sup>6</sup>, which is funded by this COST Action and from which Mr Böhm presented some work, has various goals. Among other things, the properties of carbon-based nanomaterials should be improved, their areas of application expanded and the costs of their production and application reduced. The network also aims to contribute to the EU's leading position in the field of nanoparticle-enhanced materials, promote cooperation with international companies and provide information on scientific and technological advances and challenges.

Mr Böhm explained that various additional functions of materials can be integrated into composite materials. Of particular interest for the network is the use of sensors and sensor networks to create "intelligent" material properties. This could enable advances in safety aspects, among other things. Using the example of a motorbike helmet with pressure sensors, he showed that these could facilitate the diagnosis of possible head injuries after an accident and thus improve medical assistance.

As a further example of integrated sensors, Mr Böhm presented aircraft turbines that could detect and report damage to airplane rotor blades with the help of integrated piezo-ceramic sensors. Compared to conventional systems, an important advantage is that the complicated wiring of the sensors would no longer be necessary since they

<sup>6</sup> http://www.essence-cost.eu/

have both an energy source and communication possibilities. Similar applications are possible for the rotor blades of wind turbines.

Mr Böhm mentioned some of the advantages of using these sensors in composite materials instead of using "conventional electronics":

- Complex manufacturing processes are avoided because the sensors are already integrated into the material. No complex tools or precise positioning and wiring are necessary.
- Data processing, storage and evaluation take place in the smart material and are therefore less complex; only "damage" is communicated.

Conventional electronics are often not separated into components in the waste phase. They then contaminate the material streams and make recycling more difficult. Integrated sensors also pose this problem.

Mr Böhm gave another example of the application of active, nanoscale materials: the refurbishment of concrete bridges. As an alternative to demolition and new construction, which would require large quantities of cement, bridges could be at least partially strengthened with carbon concrete, so that no new construction would be necessary, and cement and thus considerable CO<sub>2</sub> emissions could be saved. Nanoscale sensors integrated into the concrete could also measure the condition of the (repaired) bridges and report any damage. Sensors based on CNTs, graphene, carbon black or carbon fibres could be used for this "self-diagnosis of bridges".

As an example of a material or product that integrates two functions, Mr Böhm presented the structural battery for electric vehicles or aircraft. On the one hand, this is a "load-bearing component" due to the stiff and high-strength structure of the material, and on the other hand, it is an energy storage device. Structural batteries could reduce the space required and the overall weight of batteries, which could lead to fuel savings in mobility and possibly also enable the use of electrical energy as a drive for aircraft.

Mr Böhm concluded his presentation by stating that nano-reinforced composites enable multifunctional applications, but that corresponding products have not yet reached market maturity and that further support in product development and marketing is therefore necessary.

#### Discussion

It was pointed out that the use of CNTs in plastics, composites or cement can be associated with health risks, as some CNTs are carcinogenic. In addition, there are technical difficulties both in the recycling of carbon reinforced rotor blades and in



thermal recovery.<sup>7</sup> Therefore, aspects of waste management must be taken into account in the development of these products and/or new waste treatment processes are needed in order to be able to recycle the materials.

## 7 DNA as construction material for active nanomaterials

Dr Enzo Kopperger, Technical University of Munich

Mr Kopperger reiterated that DNA is a very good building material for nanoscale structures, among other things because it is both solid (double strand) and flexible (single strand).

Mr Kopperger explained how three-dimensional nanostructures can be produced: A longer scaffold strand and various (shorter) so-called clamp strands are added together. The clamp strands bind to different parts of the scaffold strand by base pairing. For this to be possible, the scaffold strand must "fold", and a three-dimensional structure is formed. This process is self-organised. The sequences of the clamp strands can be determined on the computer based on the desired structure and the sequence of the scaffold strand.

Mr Kopperger presented a structure made at the TU Munich consisting of a rod that sits on a bearing and can rotate around its axis. He explained that due to the charge of the DNA, the rod can be made to rotate with the help of a changing electrical field. It is also possible to change the direction of rotation. In order to make the rotation visible, the rod was provided with a fluorescent marker and extended in such a way that a deflection could be resolved optically.

According to Mr Kopperger, one possible application of this nanorobot could be in the field of sensor technology: By attaching a receptor molecule and binding with the target molecule, the rod would be stopped in its rotation and the fluorescence signal would be visible at one point (instead of as a circle). Compared to conventional systems, various washing steps could be omitted with such a sensor. In addition, DNA-based sensors could be produced comparatively cheaply.

Mr Kopperger added that the nanostructure could also be used as an energy storage device in a modified form along the lines of "wind-up toys". For this, instead of a free bearing, two strands would have to be used to bind the rod to the substrate (two-strand bearing). If the rod is driven electrically, its two-strand bearing would be

<sup>&</sup>lt;sup>7</sup> However, there are also research activities on the utilisation of composite materials, e.g. https://eurecomp.eu/.

twisted and mechanical energy would be stored. When the twisted strands "untwist", this energy could be translated back into a rotation of the rod.

According to Mr Kopperger, the main applications of three-dimensional nanostructures are in the field of smart drug carriers and sensors. The presented folding method of DNA allows many degrees of freedom, which could also enable mechanical processes at the nano level. Here in particular, however, research is still at a very early stage.

#### Discussion

After this presentation, several questions were asked about the stability of the structures and the possibility of activating them with a magnetic field instead of an electric field, e.g. for medical applications. Mr Kopperger explained that the structures are stable. Activation by means of magnetic fields has so far only been researched with magnets in the micrometre scale but is in principle also conceivable with smaller magnetic particles.

Some participants noted that the use of DNA was viewed with scepticism by the public, not least because of "myths" about self-replicating nanobots that could consume the Earth's biomass for their reproduction ("grey goo" scenario). Mr Kopperger replied that research was still very far away from such nanomachines.

### 8 Electroactive Polymers

#### Ivica Kolarić, Fraunhofer IPA

Mr Kolarić presented research activities on artificial muscles. Artificial muscles resemble those of humans and/or are inspired by nature but could be significantly stronger and used in a variety of ways.

Basically, according to Mr Kolarić, people and robots have so far been separated (at work) by barriers. Due to the high acceleration, people could collide with the robots and seriously injure themselves because of the stiff/hard materials. Artificial muscles could eliminate or reduce the need for this spatial separation, as they are "soft" or can soften in response to appropriate stimuli, thus significantly reducing the risk of injury.

There are various materials from which artificial muscles can be made, including metals, ionic or dielectric materials, CNTs and dielectric polymers. In his presentation, Mr Kolarić showed examples of artificial muscles made from dielectric (electro-



active) polymers and ionic actuators. The dielectric polymers function like a capacitor. They are able to relatively strongly expand and shift in space and are efficient due to their simple strucure. They can develop strong mechanical forces, whereby dielectric polymers work quickly and with high strong voltages, while ionic ones are slower but also require lower voltages and are therefore particularly interesting for medical technology.

In the medical, electroactive polymers would already be used as valves that close or open tubes as well as pumps for dosing drugs. These peristaltic pumps can be precisely adjusted and thus (continuously) dose very small amounts of medication. Furthermore, electroactive polymers are currently used as demonstrators in filter papers and wound dressings.

Possible future applications in medicine currently under development include precision tools for endoscopy or minimally invasive surgery, flexible stents, synthetic muscles for use in the body, retinal implants and, in the distant future, the production of artificial organs using additive manufacturing technologies.

Mr Kolarić also presented some possible applications of electroactive polymers in non-medical fields. One research project deals with the production of membranes that can change their shape and surface through integrated artificial muscles and that react to external stimuli. One possible application of these membranes could be in the adjustable cladding of buildings. Artificial, adjustable pores in the membranes could regulate the air exchange in the building and, using appropriate sensors, create optimal ventilation.

The combination of artificial muscles with sensors enables further applications to expand the interaction between humans and machines.

With regard to risk assessment, Mr Kolarić advocates a prospective risk analysis early on in the innovation process, the results of which are taken into account in the further development steps.

#### Discussion

In the discussion, questions were asked about the use of artificial muscles as prostheses, implants or for improving body functions ("human enhancement"). Mr Kolarić explained that in traditional prosthetics, so-called exoskeletons are used, for example, after amputations of parts of the body. However, further research is needed to use electroactive polymers in the body. Here, promising initial results were shown from work on testing sensory properties and compatibility. Mr Kolarić saw the greatest potential of electroactive polymers in the replacement of muscles and organs. For this, he said, hybrids could be produced that consist of both natural tissue and artificial muscles.

The detection of a person's intention to control muscles is very complex, as is the derivation of an appropriate reaction to it. A variety of sensors are necessary for this, as well as correspondingly complex data processing.

In the context of "human enhancement", Mr Kolarić informed about research on suits for soldiers that are supposed to support their physical abilities or protect the soldiers' lives through fibre reinforcement. Such suits could also be helpful for people with disabilities, for example. Whether and which purposes are worth supporting requires further ethical considerations.

## 9 Light against antibiotics resistance: characterization and biological properties of new photoactive materials

Prof. Dr Anzhela Galstyan, University of Duisburg/Essen

In her talk, Ms Galstyan presented how phthalocyanine-based photosensitizers can be used in the production of nanoscale materials and activated by light. The activated photosensitizers catalyse the formation of further, reactive molecules, e.g. singlet oxygen, which then have an antimicrobial or oxidative effect and can be used for various purposes.

According to Ms Galstyan, one area of application for photoactive, nanoscale materials is the disinfection of drinking and wastewater. Traditionally, additional chemicals, ozone or UV light are used for disinfection. These processes are energy-intensive and can lead to the formation of toxic substances. The use of solar-powered, photocatalytic processes could replace these procedures.

Another area of application for photodynamic inactivation of microbes could be in the health sector. Ms Galstyan saw applications for wound treatment as well as for surface disinfection as possible. Since the effect of photoactive substances is light-dependent, it could be limited both locally and temporally and thus, for example, damage to the "desired biome" of the skin could be avoided.

Ms Galstyan emphasised that the benefit of photoactive substances in disinfection was particularly that no resistance can develop. In contrast to antibiotics, the effect is very fast and bacteria and viruses, as well as the biofilms in which they reside, have no possibility to resist.

Phthalocyanines could be chemically modified, e.g. to produce a certain solubility or stability. In this way, these compounds could be used in different environments. For



this purpose, they could also be combined with nanocarriers or integrated into electrospun nanoscale membranes.

#### Discussion

In the discussion, it was explained that not only phthalocyanines, but also other photoactive molecules can be used to achieve the effects presented. Ms Galstyan explained that the type of molecule influences the degree of activity. For example, the effectiveness of phthalocyanines changes with the type of the central metal molecule: zinc, aluminium and silicone derivatives are particularly active, and some compounds are currently in clinical trials in Europe or are approved for treatment in Asia and Latin America.

Ms Galstyan explained that photoactive materials can also be used to degrade micropollutants in wastewater treatment plants. These materials could partially catalyse degradation processes that currently do not take place in wastewater treatment plants and thus improve the quality of treated wastewater.

According to Ms Galstyan, photoactive fibres in mouth and nose coverings are an application of these materials that is already on the market. It was noted that these applications do not always comply with the law, as various regulations have to be observed, including labelling as a biocidal product.

It was pointed out that there is a group restriction on the use of copper phthalocyanines in tattooing inks. This is an indication that restrictions may also be possible in other applications in the future. This should be taken into account from the outset when selecting active, nanoscale materials for possible future applications.

### **10 Regulation and ethical aspects**

## 10.1 Regulatory issues regarding active materials at the nano scale in REACH and in the CLP regulation

#### Lars Tietjen, German Environment Agency

Mr Tietjen explained that the central connecting factor in chemical law is the chemical "substance". A substance is legally defined as the product of its manufacturing, e.g. the result of a synthesis, even if from a strict chemical point of view it is mixture and not a single substance. Manufacturers and importers of substances and mixtures (intentionally mixed substances) are responsible for the safety of the products they

place on the market. In principle, the current regulatory framework works for all chemicals, including nanomaterials.

Mr Tietjen explained that the presence or knowledge of the hazardous properties of substances is the trigger for further risk management measures. Therefore, and regarding active, nanoscale materials, Mr Tietjen considered it particularly critical that:

- Some test methods are missing or not applicable: Active, nanoscale materials, like nanomaterials, can behave differently in test systems than assumed for the test method. For example, due to adsorption or, in the case of poorly soluble substances, due to sedimentation, the concentration of nanoscale materials in a test system cannot be clearly determined and it is difficult to simulate how the materials behave along their life cycle. Particulate materials, for example, are not homogeneously distributed in an aqueous test system and the actual exposure of organisms in the test system may vary. If hazardous properties cannot be determined due to a lack of test methods, regulation cannot take effect.
- Polymers are insufficiently covered in the current regulatory system, as only the monomers must be registered and tested under REACH, but not the polymers. An amendment to the REACH regulation<sup>8</sup> regarding the registration of polymers is under discussion, but until a new regulation enters into force, the information for a chemical classification is lacking. Polymers play a prominent role in active, nanoscale materials.
- Some novel materials are difficult to assign to the definitions of substances, mixtures and articles in chemicals legislation. If they are assigned to one, e.g. mixture or article, information on the hazardous properties may be missing or might not have to be generated.

Mr Tietjen presented some of the processes at EU level aimed at changing the regulatory framework for chemicals. In particular, the <u>Chemicals Strategy for Sustainabi-</u> <u>lity</u> would include various measures to realise the goals of a toxic-free environment and ending pollution. The REACH regulation would create the knowledge about chemicals on which risk management can be based.

Mr Tietjen added that innovations and the design of chemicals must already exclude possible adverse effects. One of the aims of developing a framework for assessing the safety and sustainability of chemicals (Safe and Sustainable by Design) is to support this.

<sup>&</sup>lt;sup>8</sup> Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)



#### Discussion

Some participants stated that there is a lack of transparency about the presence of substances in products in the value chain and for consumers. A respective information need was also stated from the scientific community, e.g. in order to be able to model emissions. No register on chemicals in products exists and the ECHA database (<u>SCIP</u>) was considered not sufficient to cover the different information needs. It was proposed to introduce a corresponding reporting obligation for downstream users of chemicals in order to create more transparency.

Mr Tietjen generally agreed and added that within the framework of the revision of the Ecodesign Directive<sup>9</sup> the introduction of a so-called product passport is planned, which is to provide information on the content of classified substances in products. However, he qualified that according to this (future) regulation the EU Commission is entitled to regulate individual product groups, i.e. a product passport will not be required immediately and automatically for all products. Another disadvantage was that in the proposal of the EU Commission<sup>10</sup> only substances with a harmonised classification would have to be taken into account in the product passport, but not self-classified substances. Information on substances in the environment could also be obtained via the monitoring obligations from soil protection or according to the Water Framework Directive. However, it is unclear whether and how extended or new monitoring obligations can be established.

When asked whether active, nanoscale materials, e.g. the nanorobots, are a chemical substance or an article, Mr Tietjen replied that in his opinion these structures are so small that the composition is decisive for the function. Moreover, the definition in chemicals legislation had not been worked out for these structures. Thus, in his opinion, active, nanoscale materials should be considered as substances or mixtures.

With regard to test methods, Mr Tietjen explained that tests for active, nanoscale materials had to cover all possible effects and also take into account how they change in the environment. It is necessary that the industry is more involved in the development of test methods. In addition, and in particular, industry should describe the behaviour and activity of their materials very concretely and precisely. This was

<sup>&</sup>lt;sup>9</sup> Directive 2009/125/EC of the European Parliament and of the Council of 21 October 2009 establishing a framework for the setting of ecodesign requirements for energy-related products

<sup>&</sup>lt;sup>10</sup> https://environment.ec.europa.eu/publications/proposal-ecodesign-sustainable-products-regulation\_de

reinforced by participants who saw industry involvement in test methods development as a form of exercising ownership and a way to ensure the safe use of materials.

#### 10.2 Regulatory aspects and governance

Andrea Haase, Federal Institute for Risk Assessment

Ms Haase began her presentation by stating that there is currently neither a clear definition for advanced materials nor for active, nanoscale materials and that, from a regulatory point of view, these are also not needed at present. Like Mr Tietjen, she stated that in the data collection under the chemicals regulation REACH, there is no possibility to record properties that are supposed to change during use and in response to an external stimulus. She referred to the developments in the field of nanocarriers presented earlier in the ExpertDialogue as an example of active, nanoscale materials, which, starting from applications in medicine, can now also be found in other products, e.g. in cosmetics, food, biocidal products and plant protection products.

Ms Haase informed that the Cosmetics Regulation<sup>11</sup>, the Novel Food Regulation<sup>12</sup> and the Plant Protection Products Regulation <sup>13</sup> as well as the associated guidelines for risk assessment do not contain any concrete specifications on how nanocarriers are to be assessed regarding human and environmental safety. The respective guidance documents for the regulations merely state that a safety assessment should be carried out, considering both the carriers and the "load" individually as well as the "load" and carrier as a unit.

In addition, the Plant Protection Products Regulation still lacks a definition of "nanopesticides", which is why manufacturers are currently not subject to any nano-specific requirements regarding the generation safety information. Ms Haase reported that microemulsions are already in use to increase the efficiency of plant protection products and to protect the active ingredients from environmental influences and thus make them more durable. In the context of an IUPAC workshop, a <u>proposal for a</u> <u>testing strategy</u> was developed to evaluate the safety of nanocarriers and active substances, avoiding animal testing as far as possible. The ability of the carrier to penetrate membranes and the speed of release of the active ingredient would be

<sup>&</sup>lt;sup>13</sup> Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market



<sup>&</sup>lt;sup>11</sup> Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products

<sup>&</sup>lt;sup>12</sup> Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods.

decisive in determining whether a separate assessment is necessary for the carrier and active ingredient unit, which may also involve animal testing.

Ms Haase concluded her presentation by introducing an interagency working group working on the development of an early warning system for advanced materials (including active, nanoscale materials). This working group had developed a working definition for advanced materials and described the parameters by which they consider materials to be of concern. In the early warning system, criteria are proposed for a screening step and an in-depth assessment, on the basis of which substances of increased concern can be identified. These criteria include classification under the CLP Regulation, the presence of certain properties already known to be associated with potential risks to humans and the environment (e.g. persistence or fibre form), possible release, and other sustainability aspects.

#### Discussion

In response to a question about the testing strategy, Ms Haase explained that the distribution of an active substance by a nanocarrier in the human body does not change in comparison to the "active substance" without a carrier if a) the active substances is quickly released by the carrier and b) the carrier does not cross any membranes. Only in the case of a slow release and/or the ability of nanocarriers to cross membranes does the carrier possibly influence the distribution in the body, which must then be taken into account in a test of the unit "active ingredient and carrier". Since the ability to pass through the membrane and the properties of the release from the carrier can be tested without animal experiments, this approach is helpful from the point of view of animal protection.

Ms Haase replied to the question of whether the inter-agency working group is also considering a categorisation of advanced materials that a "clustering", e.g. according to material types and functionalities, is definitely considered sensible and that this has already been discussed. A grouping in clusters can also be useful to enable joint risk assessments for several advanced materials. She pointed out, however, that unfortunately the clusters often do not allow a one-to-one allocation of all materials.

## 10.3 Ethical aspects about the use of active materials at the nano scale

#### Prof. Dr Wolfgang Liebert, BOKU

Mr Liebert presented his thoughts on taking responsibility and on ethical aspects when dealing with (active) nanoscale materials and outlined what safe and precautionary handling of nanomaterials could look like. In doing so, he opposed the tendency to formulate many new "area ethics" (such as "nanoethics"). Mr Liebert sees the core of ethics rather in being able to provide overarching orientation for the evaluation of developments rather than to consider individual areas and aspects.

According to Mr Liebert, it is a matter of taking responsibility for the consequences of one's actions - even as early as the research stage. In his view a prerequisite is an anticipatory ambivalence analysis including the clarification of intended and unintended effects of a technology, the assessment of realistic expectations versus promises and knowledge and non-knowledge about co-generated changes and consequences from technology implementation (also through possible "mass" applications) and considering the fate of substances in the entire life cycle. He considered risk assessments at the core of such considerations but found these not sufficient. Cost-benefit analyses could lead to utilitarian narrowing of the view according to him. He opines that technology assessment and design as early as possible is necessary, which also includes the examination of alternatives.

The precautionary principle is a concretisation of an ethic that demands that decisions that can prevent serious or irreversible damage should not be prevented by the lack of scientific data on the probability of the occurrence of damage or its concrete extent. The EU Commission incorporated the precautionary principle into the regulatory principles in 2000 in a communication.<sup>14</sup>

Mr Liebert explained that the approach of "safe(er) by design" attempted to grasp the intrinsic vagueness of the precautionary principle more concretely as the functionality and safety of innovations are considered throughout the entire development process. However, this approach was not sufficient for complex technology development and even the understanding of "safe" required interpretation. In addition, he criticised that other important aspects such as social values and goals are not taken into account in this approach.

Against the backdrop of increasing global environmental crises, Mr Liebert pointed out that there are also demands for a "great transformation", which is based on visions of the future that are less technology-driven but focus more on social interaction with each other and with nature, or call for general protection of living systems as an orienting principle.

<sup>&</sup>lt;sup>14</sup> Commission of the European Communities (2000): COMMUNICATION FROM THE COMMISSION the applicability of the precautionary principle, COMMUNICATION FROM THE COMMISSION the applicability of the precautionary principle.



As an example of "ethical orientation", Mr Liebert mentioned the EU Commission's recommendation of a "Code of Conduct for responsible nanosciences and nanotechnologies research"<sup>15</sup>, which contains seven principles and further guidelines. Beyond the explicit orientation towards the precautionary principle, this code of conduct specifies, among other things, the purpose of nano research (welfare and sustainable development) and calls for transparency and participation.

Mr Liebert concluded his presentation by saying that in the context of research and the handling of nanomaterials, "taking responsibility" means conducting research in an integrative, interdisciplinary and transdisciplinary manner and informing society as best as possible about safety and ethical aspects. All risks of technology must be considered along the entire life cycle and globally as well as with a long-term horizon. In addition, discursively clarified social values and norms must be used to critically examine which research and which products are really needed. He suggested basic ethical assumptions and unquestioned world views to be reviewed and, if necessary, changed.

#### Discussion

Mr Liebert's presentation was followed by a discussion on various aspects of his considerations. The following aspects were brought into the discussion by individual participants.

It was added about the approach of "safe by design" was not only concerned with safety but also linked to sustainability and socio-ecological transformation. Mr Liebert's demand for more participation of civil society in decision-making processes was supported. However, an open question was raised as to how sufficient transparency and information about complex technologies can be provided for social actors.

It was pointed out that the social value structure had changed very quickly in recent months and that legislation was lagging behind these processes. It was stated to be crucial how assessment processes (of technologies) are implemented. Furthermore, it was reminded to recognise what has already been achieved, e.g. that risk assessments and life cycle considerations are prerequisites for the approval of funding in EU research programmes.

Regarding the Code of Conduct of the EU Commission, it was added that it had been developed jointly by the industry, a bank and the regulators. However, the binding

<sup>&</sup>lt;sup>15</sup> European Commission, Directorate-General for Research and Innovation, Commission recommendation on a code of conduct for responsible nanosciences and nanotechnologies research & Council conclusions on responsible nanosciences and nanotechnologies research, Publications Office, 2009, https://data.europa.eu/doi/10.2777/28456

implementation failed because the implementation of the principles and guidelines was not considered controllable (no monitoring). It was thus decided that the Code of Conduct could not be made mandatory.

In response to the comment that researchers themselves would also decide which projects and work they undertake and consider meaningful, Mr Liebert objected that individual researchers should not be overburdened. He believed the current system of evaluating research performance does not encourage the incorporation of ethical considerations into research decisions and collective learning about the possible consequences of innovations. Moreover, it would not (or no longer) be possible for individuals to assess the consequences of an innovation, as these are too complex and interconnected. Therefore, it is important not to leave these assessments to the individual.

Another participant confirmed that the term "safe" is interpreted differently and that the application context must be considered in each case. In general, the reaction to innovations in Germany would be rather cautious, which the person attributed to the fact that the occurrence of negative effects of technology is considered more probable or more significant than the expected benefit.

Mr Liebert's statements, which expanded the ethical perspective on the basis of the future of the planet as a whole, were seen as unhelpful in one contribution. It was claimed necessary to be able to also look at and evaluate individual aspects of a development.

Another contribution dealt with the question of whether it is important to already deal with many aspects of ethics and impact assessment in education so that it is possible to recognise knowledge and non-knowledge at all. Deficits were noted in Germany in this regard with an ask for them to be remedied in order to be able to assess and decide better in the future. It was observed that chairs of toxicology were being abandoned in universities in favour of chairs of pharmacology. This was described as unfavourable.

It was further cautioned that it is a fallacy that the research on nanosafety, which has now been ongoing for some time, has already resolved all issues. It was stressed that this is not the case, and that work should continue to ensure appropriate regulation and responsible use of nanomaterials.



## 11 Summary

The ExpertDialogue "Opportunities and risks of active materials at the nano scale", gave an overview of these materials and introduced to possible areas of application. Presentations on the legal situation and ethical considerations rounded off the event.

Active, nanoscale materials can perform many different functions. Functions from the macro level are transferred to the nano level, but properties of the nano range, such as plasmon resonance, are also used. Active, nanoscale materials can react to external stimuli and change their energy state, composition, or structure during their use. They can be made of organic or inorganic compounds or a combination of both. In many areas, polymers such as DNA are used to create nanoscale structures.

There is no clear definition for active, nanoscale materials. The proposal by Camboni et al.<sup>16</sup> seemed helpful to some participants but was also criticised because of possible borderline cases.

Currently, active, nanoscale materials seem to be developed predominantly in and for medicinal applications. Nanocarriers have already been in use for a long time and are used to bring pharmacological agents to their site of action in a stabilised and/or targeted(er) manner. In addition, active, nanoscale materials seem to be well suited as sensors. Various detection principles based on the activity of nanoscale materials were presented at the ExpertDialogue.

For most of the applications presented, the materials are still in the research or development stage and have not yet reached the market.

The opportunities of using active, nanoscale materials lie on the one hand in an increase in efficiency and/or cost reductions for certain processes: nanocarriers can lead to higher concentrations of active substances at the sites of action, diseases can be diagnosed more quickly, components can be manufactured more simply, and materials can be saved. It is possible to become more precise, e.g. in dosing pumps based on artificial muscles or to combine several functions in one material, as the example of the structural battery showed. Particularly in the medical field, completely new qualities are being achieved, e.g. by "packaging" in carriers, active substances can be used that would otherwise be degraded in the body. However, little is known about the possible risks of these carriers.

<sup>&</sup>lt;sup>16</sup> Camboni et al. (2019) A State of Play Study of the market for so-called "Next Generation" Nanomaterials. European Chemicals Agency, Ref.-No. ECHA-2019-R-14-EN, ISBN: 978-92-9020-726-9, DOI: 10.2823/242422, pp. 25-26. Passive nanomaterials, nanostructures and nanostructured materials are distinguished from active ones in that the former are in a thermodynamically metastable state and changes in state are not intended. The latter are referred to as (re-)active nanomaterials, nanostructures and nanostructures and nanostructures and nanostructures energy during use, converting it into non-equilibrium state activities that are often, but not always, associated with movement, growth or propagation.

Other opportunities for the application of active, nanoscale materials include reduced side effects of medicines, the possible replacement of toxic heavy metals, the extension of the service life of materials and the associated reductions in resource consumption, as well as increased safety due to the possibility of continuously monitoring materials' integrity with sensors.

The risks of using active, nanoscale materials are closely linked to which building blocks they are made of. For example, some CNTs are carcinogenic, tungsten oxide is considered genotoxic. Phthalocyanines are partly restricted in tattoo inks due to sensitising and other hazardous properties.

Some applications use rare raw materials; for example, indium phosphide as quantum dots, which cannot be recovered after use. Materials that consist of several components and/or are very complex could disrupt waste treatment in the future or make recycling more difficult. Here, carbon-reinforced rotor blades of wind turbines were mentioned as an example of materials, for which an appropriate waste processing is not yet available.

Many of the materials of organic origin, e.g. DNA, are considered low-risk because degradation mechanisms exist in the body and the environment. However, it is unclear whether the superstructure of the materials changes their behaviour or degradation in humans and the environment. The existence of harmful properties of (synthetic) polymers was not reported at the ExpertDialogue.

The existing chemicals legislation is in principle suitable for regulating active, nanoscale materials in such a way that they can be used safely. However, information about the (hazardous) properties of the materials must be known. This requires corresponding obligations for the manufacturers of the materials as well as applicable test methods. At present, polymers, many of which are also used at nanoscale and in active materials, are not subject to registration under REACH and many established test methods are not applicable to nanomaterials and active, nanoscale materials. Thus, it cannot currently be ensured that risks can be identified and regulated. In addition, it is unclear whether there is adequate guidance on risk assessment. Legislation on cosmetics, novel foods, biocides, and plant protection products does currently contain provisions on nanomaterials. However, concrete guidelines on how to assess the risks of nanocarriers are missing.

The ethical assessment of the application of active, nanoscale materials is complex. The identification of possible risks and trade-offs with expected benefits is a task that can only be tackled collaboratively due to the multiple interactions of the technologies with different areas of society and the current rapidly changing values.

The ExpertDialogue shed light on active, nanoscale materials and gave participants an insight into research into their application in various fields.

