Synthetic nanoparticles and the precautionary principle
An ethical analysis

Andreas Bachmann, Ethik im Diskurs

1. Introduction

Nanotechnology is commonly considered today as one of the key technologies of the 21st century. It is recognised to have great potential, both economically and scientifically. At the same time, it is still largely unknown to the general public. This is due not least to its having undergone constant but relatively unspectacular development. There has been no revolutionary, high-profile breakthrough, nor any serious incidents or setbacks.

One problem of this development is that more and more nanoproducts are coming onto the market without consumers being aware of it, and without anyone having an overview of these products, since they do not require approval or labelling.

This situation is problematic, especially because initial toxicological tests have indicated that nanoparticles may harm humans and the environment. The need for an ethical evaluation of the risks associated with the manufacture and use of these particles has therefore become urgent.[1]

I shall put forward the thesis that this ethical evaluation should follow the lines of the precautionary principle. The precautionary principle says that appropriate precautionary measures limiting the freedom of research and companies are justified, if a (new) technology threatens severe and irreversible harm to humans and the environment, even if no established scientific risk analysis is available.

It is uncontested that there are uncertainties and gaps in our knowledge of possible adverse impacts of nanoparticles. Nevertheless, research on risk has made advances in recent years.[2] It has reached a point where an interim assessment of the potential risk can be undertaken, at least for some nanoparticles. Initial results indicate that nanoparticles such as nanotubes and buckyballs are particularly associated with substantial risks to human health and the integrity of the environment. However, not everyone shares this assessment. There are also opposing voices who say that, although some indications of the potential danger of these and other nanoparticles for humans and the environment can be recognised, there is no reason to have serious concerns (Brune *et al.* 2006:376). Using a few recent toxicological studies, I will show there are indications that this judgment may not be accurate.

If it is correct that at least some synthetic nanoparticles can cause severe harm to humans and the environment, and if the application of the precautionary principle is therefore justified, the question arises of which precautionary measures should be taken. The answer to this question is: it depends who is exposed to the risk, and in what way. It is one thing when researchers in their laboratories handle relatively small amounts of nanoparticles in contained systems, but quite another when such particles are produced in factories by the ton, and still another when non-involved third parties, such as consumers of nanoproducts, come into contact with them. According to the type of risk exposure, and depending on whether the nanoparticles in question are free or bound nanoparticles, different measures are required by the precautionary principle: some precautionary measures to minimise risk, and some prohibitions. It is important to point out that these are temporary measures that are justified

[1] The author would like to thank Ludwig K. Limbach, Olivier Sanvido and Luis Tiefenauer for further suggestions and critical comments.
[2] Links to the latest essays in this field can be found on the International Council on Nanotechnology (ICON) website (http://icon.rice.edu/research_archive.cfm?mode=yearly&year=2006).

only in relation to the current state of knowledge. Reappraisals and revisions should be undertaken if new research findings indicate that the danger to humans and the environment associated with synthetic nanoparticles diverges significantly from what has previously been assumed.

2. What are synthetic nanoparticles and how are they significant for nanotechnology and nanobiotechnology?

There is as yet no generally accepted definition of nanotechnology. For our purposes, it is enough to indicate that three features are constitutive of this technology:

1. The size: nanotechnology concerns structures at the nanometre scale. This extends from 1 to 100 nm (where 1 nm is one billionth of a metre)
2. The utilisation of new effects that occur in materials at nanoscale
3. The selected production and/or manipulation of nanoscale structures.

In terms of size, materials with two or three dimensions at the nanoscale level play a central role in nanotechnology. These materials, nanoparticles, are characterised by two properties that make them particularly interesting in new applications and products:

1. They have a greater surface-to-volume ratio (per unit mass) than non-nanoscale particles of the same material, and are therefore more reactive.
2. If they are smaller than 50 nm, they are subject to the laws of quantum physics, with special quantum effects.

These properties explain why any material can behave quite differently at nanometre level: it may change its colour, suddenly become soluble, or suddenly show conductive behaviour. To give one example, nanoscale titanium dioxide – in contrast to non-nanoscale titanium dioxide – is not only transparent, but also a very effective UV blocker, which is why it is used in sunscreens.[3]

I do not examine all nanoparticles in detail below, but only a particular class. These are synthetic nanoparticles (also referred to as ‘engineered’ or ‘manufactured nanoparticles’). Synthetic nanoparticles are characterised by having been produced with the intention of using their special properties for very particular purposes. They should be distinguished from a) nanoparticles produced by natural combustion processes, such as forest fires; and b) nanoparticles that are the unintentional by-products of human-induced combustion processes, such as cigarette smoking.[4]

The most important synthetic nanoparticles with two dimensions at nanoscale level are ‘nanotubes’. Nanotubes are tube-shaped arrangements of carbon atoms with a diameter of a few nanometres. They are considered *the* material of the future. This is due to their extraordinary properties: they are a hundred times stronger and five to six times lighter than steel; at the same time they are flexible and plastic, and conduct heat and electricity extremely well. They could, for example, be used in the manufacture of transistors for computer chips, monitors or sensors; or even for hydrogen storage. They could also find applications in many building materials, in the construction of aircraft and cars, or in bone implants and artificial joints. They are already being used in tennis balls and extremely light and stable tennis rackets, as well as in batteries.

A whole range of nanoparticles have three dimensions at the nanoscale. The following should be mentioned in particular:

[3] Non-nanoscale titanium dioxide is also a UV blocker; but it is white, not transparent.
[4] a) and b) are generally referred to as ‘ultrafine particles’. Nanoparticles’ therefore primarily refers to synthetic nanoparticles.

- Buckminsterfullerenes. Named after the American architect Buckminster Fuller, who became famous for his geodesic domes, they are the third form of pure carbon, next to graphite and diamond. They are a group of carbonaceous cage-shaped molecules, of which the most important is the C_{60} molecule, which resembles a geodesic dome. This molecule, with a diameter of about 1 nm, is also called a 'buckyball'. Such buckyballs could be used, for example, as drug delivery vehicles, i.e. to transport substances to a precise target, or in electronic circuits.
- Quantum dots: are extremely small, pyramid-shaped particles of semiconductive materials. They are used, for example, in the production of high-resolution flat screens in televisions or computers, in very light and longer-lasting batteries, and in new types of laser system. In molecular imaging they are employed to visualise individual molecules. For this they need a suitable coating, as their core is generally made up of poisonous heavy metals such as cadmium selenide.
- Carbon black: has already been used for some time as a reinforcing liner material in rubber tyres.[5]
- Metallic oxides such as SiO_2, TiO_2, Al_2O_3, ZnO, Fe_2O_3 and Fe_3O_4. Metal oxides can be used for very varied purposes, at the moment primarily for improving existing products such as cosmetics, sunscreen and food packaging.
- Metals such as gold and silver. Nanosilver particles, for example, are used in medicine to prevent infections because of their antibacterial effect (in wound treatment, nanosilver-coated catheters etc.). The ability of nanosilver to purify drinking water is being tested.
- Semiconductors such as cadmium telluride (CdTe) and gallium arsenide (GaAs).

These few possible applications alone make it clear how significant synthetic nanoparticles are for nanotechnology in general, and for nanobiotechnology in particular. Synthetic nanoparticles play a central role in nanobiotechnology, which links research into biological and non-biological systems at nanoscale in various fields. Above all, delivery technology is considered to have great potential. The idea on which this technology is based is as simple as it is attractive. It consists in using nanoparticles as a means of transport, bringing very varied active agents precisely to their site of action, and releasing them there in a controlled manner. In medical research, intensive work is currently being done primarily in the development of drug delivery systems. These would bring the old dream of the targeted employment of medical agents, which makes drugs significantly safer and more effective, one step closer. Using delivery technology is also imaginable in other fields. For example, once functional it could be used to transport vaccines, pesticides, food additives, or toxic substances in bioweapons.

So synthetic nanoparticles have a great potential in a range of applications. How far this potential can be exploited, and how much time is needed, cannot yet be estimated. Here it is important to focus not only on the opportunities associated with the use of synthetic nanoparticles, but also on the risks. For nanotechnology will receive social acceptance in the long term only if its products are believed to be safe as well as useful. From an ethical standpoint we should undertake an evaluation of the risks of synthetic nanoparticles now, i.e. with nanotechnology still in its infancy. For it is becoming apparent that over the coming years, more and more nanoproducts will be thrust onto the market, and we cannot say with sufficient certainty that they are harmless for humans and the environment.

Considering the potential risk of synthetic nanoparticles, three aspects should be emphasised:

[5] Including carbon black in this list is however contentious: some researchers do not consider it to be a synthetic nanoparticle.

1) There are still substantial uncertainties and gaps in our knowledge of the risks of these particles to humans and the environment.
2) Nevertheless, risk research has advanced in recent years, largely through in vitro and in vivo studies, which permit an empirically based, interim – and correspondingly tentative – risk assessment. This shows increasingly clearly that at least some synthetic nanoparticles are able to cause severe harm. At the same time it has also become clear that we cannot make sweeping generalisations, but must analyse each particle separately.
3) If we consider the key properties of synthetic nanoparticles, in particular their size, surface-to-volume ratio and the associated higher reactivity, the results of risk studies performed to date are unsurprising.

I will explain these three points in greater detail below. It is particularly important to view what is already known from scientific investigations, because the application of the precautionary principle can be justified only if there is empirical evidence that synthetic nanoparticles really can cause severe harm.

Nanoparticles are characterised by a large surface area in comparison to their volume. This indicates high reactivity. In general, the more reactive a substance is, the greater its toxicity. However, we should be careful here. In addition to the surface area, other factors such as size, shape, surface structure and solubility can also affect toxicity (Brunner *et al.* 2006). Thus, we cannot deduce from the bald fact that a particle is a nanoparticle, that it is toxic. On the other hand it would be curious if, based on the properties mentioned, nanoparticles were to prove completely harmless. It would be sensible to presume that these particles have a certain fundamental hazard potential. For this reason alone – and because we cannot extrapolate the effects of nanoparticles from the known effects of the same substances at micro or macro level – care is required in handling them.

But it is important that we avoid hasty generalisations. Whether nanoparticles are toxic, and if so how toxic they are, must be tested on a case-by-case basis.[6] There are still major gaps in our knowledge here. We have little substantiated evidence on which nanoparticles at which size or dose could harm humans or animals.[7] Still less do we know what impact the release of nanoparticles would have on the environment – plants, microorganisms, ecosystem processes – and what consequences this would have on the food chain. There is therefore general agreement that research into these risks should be intensified.

This does not, however, mean that we are entirely ignorant. On the contrary: in recent years, our knowledge of the risks posed by synthetic nanoparticles has been extended through a growing number of toxicological studies. Although these studies leave many questions unanswered, they show quite clearly that at least some synthetic nanoparticles are able to cause severe harm.

3. The risks[8] of synthetic nanoparticles for humans and the environment: current state of knowledge

3.1 Bound v. unbound nanoparticles

[6] It is unclear at present whether particular particles behave similarly, if so which ones they are, and whether this enables us to place nanoparticles in risk classes, which would then enable some complex and time-consuming case-by-case analyses to be omitted.

[7] In addition to catalysing undesired chemical reactions such as the formation of free radicals, there are two other kinds of toxic effect: the 'release and incorporation of toxic ions from incorporated particles', and 'mechanical effects in analogy to asbestos fibres' (Tiefenauer 2007:15).

[8] One special risk, which is not considered further below, is that of explosion. The higher surface reactivity and the surface-to-volume ratio of nanopowders increase the risk of dust explosions (Renn/Roco 2006:43).

The differentiation between bound and unbound (i.e. free) nanoparticles is fundamental to an analysis of the risks associated with nanoparticles in general, and synthetic nanoparticles in particular. Bound nanoparticles are firmly integrated into a vehicle and are therefore insulated from the environment. One example is materials with self-cleaning or anti-adhesive coatings. 'Although these materials owe their properties to nanoparticles, the latter are anchored in a matrix of plastics' (Boeing 2005:35) and are therefore harmless to humans and the environment. It is different for unbound nanoparticles, as they can interact with cells and thus cause harm. This is particularly the case for synthetic nanoparticles such as buckyballs and nanotubes, which are not bound into a matrix.

When I refer to synthetic nanoparticles below, I mean such free – i.e. unbound – particles. I am assuming that they exhibit the following additional properties:

- Unless otherwise stated, they exist in non-agglomerated form, because it is principally in this form that they are of interest to nanotechnology.
- They are uncoated, i.e. they lack coatings to reduce the toxicity that would be present in the uncoated state.
- They are insoluble and not biologically degradable, because otherwise they could dissolve or degrade before setting off a toxic reaction.

There are three possible ways in which bioactive particles of this kind could cause cell damage:

1. By causing oxidative stress inside the cell or on its surface: 'This means that free radicals form, i.e. molecules with a free electron, which are thus extremely reactive. The result is that the calcium level inside the cell rises, and the unwanted transcription of genes into proteins within the cell nucleus may be activated. Proteins can then cause tissue inflammation' (Boeing 2005:37).[9]
2. Receptor molecules on the cell envelope are activated because metal atoms detach from the nanoparticles. The consequences would be the same as in case 1.
3. 'The nanoparticle is swallowed whole by the cell and may enter the mitochondria, the "power houses" of the cell. Their activity is disturbed by the presence of the particle' (Boeing 2005:37).

3.2 Risks of synthetic nanoparticles for humans and animals

Let us first consider the risks posed by synthetic nanoparticles to human and animal health. In view of the route of entry of nanoparticles into the human or animal body, the available in vitro and in vivo studies give the following picture (Borm *et al.* 2006):

- Nanoparticles have almost unlimited access to the body. They can enter the bloodstream through breathing (lungs) and via the digestive tract, and from there reach all the organs (liver, spleen, bone marrow etc.).
- It is unclear whether absorption can take place through the skin. This appears to be almost impossible for normal skin; but it is unclear what happens if the skin is damaged, for example by eczema. There are also indications that nanoparticles could pass via the skin into the lymphatic system and lymph nodes.
- Under certain circumstances, some nanoparticles can cross the blood-brain barrier.
- Nanoparticles can enter the brain directly via olfactory nerve fibres in the nasal mucosa. It is not known how they behave there.
- Nanoparticles can penetrate cell membranes and reach the cell nucleus.

Even if we do not know precisely how (insoluble) nanoparticles behave in the human body, the fact that they are capable of spreading throughout the body, interacting with cells and crossing the blood-brain barrier, is a further reason for care and caution when handling them. It is certainly the case that both natural and synthetic nanoparticles have a tendency to

[9] See also Limbach *et al.* 2007.

clump, i.e. aggregate into botryoid agglomerates. This means that, above a cluster size of one micrometre, their reactivity decreases. They are then also too large to enter the bloodstream via the lung. Toxic effects based on small size and high reactivity are then no longer significant. But in most cases, synthetic nanoparticles in particular are useful only if they do *not* clump. A special coating is added to the nanoparticles as an attempt to prevent clumping. This means that these particles remain reactive and highly mobile, and thus potentially toxic (even if toxicity is reduced by the coating).

In vivo toxicological studies have so far been performed primarily in rats, mice and fish. These studies make it clear that synthetic nanoparticles are potentially severely harmful:

- Various studies have shown that fullerenes and nanotubes, in particular, cause inflammation in the lungs if they are inhaled at a certain (high) dose (see, for example, Bottini *et al.* 2006). This also applies to substances such as gold, carbon black and TiO_2,[10] which are normally harmless but can be toxic in nanoscale form.
- The well-known – if not entirely undisputed – experiment by Eva Oberdörster using largemouth bass showed that the uptake of buckyballs in these fish caused severe brain damage within 48 hours (Oberdörster 2004).
- One study from 2006 (Long *et al.* 2006) shows that the higher reactivity of nanoscale titanium dioxide can damage the microglia, which protect the central nervous system, through oxidative stress due to the formation of free radicals.
- The results of a recent Chinese study (Chen *et al.* 2006) using nanoparticles of copper in mice included the following: 'Nanoparticles induce gravely toxicological effects and heavy injuries on kidney, liver and spleen of experimental mice, but micro-copper particles do not, on mass basis'. In general, these particles are classified as class 3 (moderately toxic), in contrast to micro-copper, which is practically non-toxic. In addition, the toxicity is sex-dependent: male mice showed more severe toxic symptoms than females at the same particle mass.

Naturally, there is a question of whether and how far these results can be transferred to humans. There are indications that extrapolation would be problematic, as the process of particle inhalation is different in rats than in humans and other large mammals: they appear to react more sensitively but have a more active immune system that breaks the particles down more quickly. In the few direct measurements undertaken in humans, however, it has been shown that certain risk groups, such as asthmatics, react more sensitively than healthy people to adventitious nanoparticles.

Moreover, in vitro experiments with human cells suggest that synthetic nanoparticles, especially nanotubes and buckyballs, may severely harm human health. For example, it has been shown that a certain concentration of buckyballs causes 50% of human skin cells to die.[11]

Researchers at EMPA discovered in 2006 that nanotubes are especially harmful to lung cells when they clump together in a larger, needle-like form. Cell biologist Peter Wick says: 'These agglomerates are similar to asbestos fibres – in both their appearance and their toxicity … they appear, therefore, not to be completely harmless' (EMPA News 2/2006).

Finally, it should be noted that even uncoated quantum dots can be toxic, i.e. can cause cell damage. This is because their core consists of toxic heavy metal compounds such as cadmium selenide.[12]

---

[10] 'For poorly soluble, low-toxicity dusts such as titanium dioxide, smaller particles in the nanometre-size range appear to cause an increase for lung cancer in animals on the basis of particle size and surface area' (Schulte 2007:6).

[11] If they are coated with certain molecules, on the other hand, the effect is less toxic. The coating prevents oxygen and water molecules or ions interacting with the radicals of the carbon atoms in the buckyballs.

[12] Cytotoxicity does not appear to be completely neutralised through coating. There is also the question of what happens if the quantum dots persist in the body and their coating degrades.

In summary, we can say that certain toxic effects of synthetic nanoparticles such as buckyballs, nanotubes and quantum dots have been demonstrated in experiments on animals and on human cells. How they might damage human health, however, has not yet been sufficiently clarified. Nevertheless, the in vitro and in vivo experiments already performed suggest there are reasonable grounds for assuming that synthetic nanoparticles are also dangerous to humans and can cause similarly severe harm as in animals and human cell cultures, particularly when they enter the body in large quantities.[13]

3.3 Risks of synthetic nanoparticles for the environment

As yet there is little solid evidence concerning the impact of synthetic nanoparticles on the environment, especially their ecotoxicity and the consequences for the food chain. Some of these findings, however, are disturbing.

- A study performed in 2005 showed that nanoparticles from clay, which are already in use, can disturb the root growth of certain plants (Yang/Watts 2005).
- There are indications that buckyballs are bioaccumulative, i.e. they have a tendency to be deposited in the body at increasing concentrations through the food chain (Locatelli *et al.* 2005:32).
- It is known that nanoparticles tend to clump. Clumped particles such as buckyballs can (in water) be toxic to bacteria (Borm *et al.* 2006, Locatelli *et al.* 2005:30).
- Silver nanoparticles, which appear to be harmless for humans, can be highly toxic to useful bacteria and aquatic organisms (Weiss 2006).
- Nanoscale titanium dioxide is highly reactive, i.e. it chemically creates 'hot' free radicals, which are capable of destroying bacteria. Some experts are therefore concerned about the impact of these particles on soil ecology, if they enter the environment in substantial quantities. The same concern applies to the environmental release of buckyballs (Locatelli *et al.* 2005:27).
- It is conceivable that the small size of nanoparticles increases their mobility. Since unbound nanoparticles are generally very reactive, it can be assumed that they bind with other substances in the environment, possibly also poisons, and because of their mobility could disperse these widely.[14] How this risk should be assessed depends on how long they remain active, as well as on their mobility. Initial tests with ferrous nanoparticles have shown that these particles are (re)active in soil and in water for several weeks.

What impacts unbound synthetic nanoparticles have on plants, microorganisms and ecosystem processes could become clearer should they be used to remediate large-scale contaminated sites, as is already being done in a rudimentary way in the USA. The idea behind it is:

---

[13] A further danger is that the overall surface and overall number of particles could overload the macrophages – the immune system's 'eliminators'. 'This "overload" triggers stress reactions, which causes inflammation of the surrounding tissue. Worse, the phagocytes withdraw into deeper layers of tissue and are thus no longer present to perform their function. Successive particles are retained and can exert their reactive effect fully. Other invading pathogens, such as bacteria, cease to be effectively combated as well.' (Swiss Re 2004:16). Oberdörster *et al.* also state (2005:824): 'The extraordinarily high number concentrations of NSPs per given mass will likely be of toxicologic significance when these particles interact with cells and subcellular components. Likewise, their increased surface area per unit mass can be toxicologically important if other characteristics such as surface chemistry and bulk chemistry are the same.'

[14] Nanoparticles are able to bind pollutants and transport them through the soil. Assuming that they are very mobile because of their size, 'pollutants could be absorbed by various earth strata in larger quantities and at a faster rate. This might mean that the ordinarily less mobile fertilisers and pesticides in the soil could be transported "piggyback" style over long distances by the mobile nanoparticles. Given that such particles tend to be very reactive, various reactions with substances present in the environment, and leading to new and possibly toxic compounds, are conceivable.' (Swiss Re 2004:29).

‘Skirting the expense of pumping up and treating polluted groundwater, reactive nanoparticles could be pumped into the soil to transform pollutants – such as organic solvents or heavy metals – into harmless substances by means of a chemical reaction. … New, nanotechnological environmental techniques are based on the application of artificially manufactured, highly reactive nanoparticles which, because of their small size, can have a total surface area measuring up to 1,000 square metres per gram. This active surface area can enter into a chemical reaction with certain toxic contaminants in the soil, groundwater or air and “neutralise” them. Further, nanoparticles that contain silver and have an antibacterial effect are currently being tested for processing drinking water. … Similar cleaning methods are also under discussion in connection with the contamination caused by industrial manufacturing and processing techniques. In this area, the use of nanotechnology focuses on environmentally benign, industrial manufacturing processes in which toxic exhaust fumes and other process-related secondary products are decontaminated by nanoparticles.’ (Swiss Re 2004:27)[15]

Günter Oberdörster, one of the world’s leading nanotoxicologists, points out here that tests should first be performed to clarify whether these nanoparticles are harmless. Such large-scale injections of nanoparticles into the environment could have severe impacts on flora and fauna – and thus on the food chain as well. He also warns against being too optimistic: it is not clear that the nanoparticles in question move quickly enough through the soil or water to fulfil their intended purpose (Oberdörster *et al.* 2005:825).

Although there are still major gaps in our knowledge of the ecotoxicity of synthetic nanoparticles, the existing findings allow us to conclude that particles of this kind, particularly in substantial quantities, can cause significant harm to the environment. The careful and prudent handling of synthetic nanoparticles therefore appears necessary, not just for the sake of humans, but also to protect the natural environment around us.

But what does that mean in concrete terms? What measures should be taken to protect humans and the environment in an appropriate way from the risks of synthetic nanoparticles? In response, I believe we should follow the precautionary principle. In its most general form, this principle can be formulated as follows: to prevent imminent harm to humans and the environment, the State is legitimised even under conditions of scientific uncertainty in taking appropriate precautionary measures, which may limit the freedom of companies and of research.

This formulation requires explanation and clarification. First, we must remind ourselves of the ethical foundations, or the ethical core, of the precautionary principle, and reflect on some of the fundamental issues of risk ethics. Against this background we can then consider general conditions for applying the precautionary principle, and the two essential ways of reading the principle (4). Only when this preliminary work has been done can we answer the question of what this means in practice for the handling of synthetic nanoparticles (5).

4. The ethical foundations and conditions for applying the precautionary principle

Risk ethics is concerned with the conditions under which a person may expose him or herself and others to a risk (Bachmann *et al.* 2006, Hansson 2007, Rippe 2002, Rippe 2006). Risks are characterised by two variables: probability and harm, or magnitude of harm. In order to determine them, both variables must always be considered and linked with one another. For

[15] In addition to water purification and the decontamination of polluted soils, it is hoped that progress will be made in environmental protection thanks to the energy-saving potential of nanotechnology and nanobiotechnology.

example, the risk of being killed concerns great harm. We can describe the risk as slight only if the probability of this event occurring is extremely small.

Exposing other people to risks through one's actions always requires justification, because there is a defined probability that the action may cause them harm. This applies irrespectively of whether harm does occur (and independently of the extent of the harm). For example, if a person drives at excessive speed through a residential area, this is morally wrong because he or she is exposing the children who live in this area to a risk that is too high. This behaviour is wrong even if nothing happens to any of the children. The formulation 'risk that is too high' indicates, however, that it is not always morally bad to expose others to a risk. Under certain conditions it may be permitted and therefore be ethically justified.

It is in everyone's interest to accept some risks, as long as certain conditions are fulfilled. There are two reasons for this. First, if only actions that exposed no one to risk were permissible, the result would be a general blockade on action, which would make living together in society impossible – and this cannot be in the individual's interest. It also explains why some of the pertinent risk-ethical criteria are inappropriate as general criteria for risk exposure, e.g. the maximin criterion and the consent criterion. Both criteria are too restrictive, if ethical criteria are expected to enable and shape social coexistence. Maximin would mean always acting in such a way that the greatest possible harm is avoided. But this would make daily actions practically impossible. This also applies to the consent criterion. If consent had to be obtained for every action that exposed another person to a risk, the result in practice would be paralysis.

Second, however, exposing someone to risk and being exposed to risk is often an asymmetric situation. The question therefore arises of why the person who is exposed to a risk without benefiting from it – the exposed person – should accept it, if the person responsible for the exposure is not at risk him/herself. They have reason to do so only if the exposer behaves in a certain way. Then, although the situation remains asymmetric, it is generally in the exposed person's interests to accept the risk, since that person must assume that he or she will in turn expose others to risks in many situations, and that it is then in his or her interest if the others accept this in their turn.

The decisive condition is that the exposer takes appropriate measures of care and precaution. 'Appropriate' means that these measures should reduce the risk of the exposed person as far as is practically possible. 'Practically possible' means that they must not be so costly und comprehensive as to reduce our room for manoeuvre to zero. It must be possible to integrate them into daily life. If these measures have been taken, the person responsible for the exposure cannot be morally blamed if harm does occur. Herein lies the ethically acceptable 'residual risk': the harm may occur, even if the exposer has taken appropriate precautionary measures. If harm occurs because the exposed person has been careless, it cannot be blamed on the exposer. The exposed person alone caries the responsibility and is in this way 'to blame'. Naturally, this does not mean that they are morally obliged to act carefully or with precaution. Rather, it is simply in their own interests. If they do not behave appropriately, they are acting against these interests. This is imprudent but not morally wrong or reprehensible.

This risk justification model works only if the probability of harm occurring, as well as the type of harm or the extent of harm, can be reliably determined – in short, if we are dealing with known risk for which we can prepare. For only if we have sufficient scientific or general experience of a risk can the exposed person take precautions in order to minimise the risk, and also monitor whether the exposer really has taken the necessary precautionary measures.

For the handling of synthetic nanoparticles, this condition is not – or is only partially – fulfilled. The associated risks are new ones. It is not clear what an exposed person (particularly outside laboratory conditions) can do to adapt to these risks; neither is it clear what precautionary measures the exposer should take in order to prevent harm occurring.

Nevertheless, we are not in a situation of total ignorance; the situation should rather be characterised as one of uncertainty. There are empirical indications that at least some synthetic nanoparticles are dangerous; and there are also indications that the potential harm could be severe. But it is unclear what harm could occur, under what conditions, and with what probability; nor why it happens. The precautionary principle is intended to cover exactly these novel risks, which are associated with potentially severe harm.

Let us attempt to state precisely what we mean.

It is doubtless sensible, and morally right, for caution to prevail on the roads: we should wear seatbelts to reduce the health risks to ourselves, even if the probability of accident is minimal; we should adapt our speed to the circumstances, in order to reduce the risk to others (pedestrians, cyclists). In this sense we should avoid doing anything that entails potential harm or increases the probability of harm occurring. We are talking about taking precautionary measures, based on broad experience or statistically supported knowledge. If these measures are taken, the corresponding risk of causing harm to others is permissible, as long as benefits associated with the action (e.g. driving a car) outweigh the reduced but still present risk. These measures are not, however, intended for situations of uncertainty, but for those in which it can clearly be determined what should be done in order to protect oneself and others from unnecessary risk.

This does not mean striving for total safety and therefore reducing risk to zero. Taken literally, this is unachievable – and so it makes no sense to link the requirement for caution to it. Even the precautionary principle (in its strong version) does not require the proponents of a hazardous technology to prove its total safety before it can be considered permissible. If this were a requirement, the precautionary principle would effectively prohibit all the technologies, products and behaviours it covers, because total safety and therefore zero risk can fundamentally never be achieved. Medicines and food additives, for example, would no longer be permitted. This effect would make the precautionary principle completely unreasonable.

Looking at the history of the precautionary principle (Rippe 2002, Sandin 2007, Sunstein 2007), its purpose becomes clearer. The core idea is that if long-term severe and irreversible harm threatens humans and the environment, the lack of substantiated scientific evidence cannot be a reason for the State to postpone implementing suitable regulatory measures to prevent or minimise the corresponding risks. Put positively: in these cases the State may legitimately take, and may even be obliged to take, appropriate precautionary measures. This can mean that it correspondingly limits the freedom of researchers or companies. Conceived originally for environmental protection, the precautionary principle has since been extended to many socially relevant fields of action.

There is unity on one point: State measures are justified in the event of imminent harm, even if there is (as yet) no conclusive scientific proof of risk, as long as the measures themselves do not create greater risks than the risk they target. The precautionary principle thus covers situations of uncertainty. Uncertainty is a particular type of risk in which the extent of the harm and the probability of the harm occurring cannot be calculated with complete certainty, but can be roughly estimated. More precisely, there are three types of uncertainty: 1) The extent of harm is known objectively, but the probability can only be estimated subjectively. 2) The probability is objectively known, but the extent of harm can only be estimated subjectively. 3) Both the probability and the extent of harm can only be estimated subjectively.

How we classify the risks of synthetic nanoparticles in our current state of knowledge depends on how we interpret ‘subjective’ and ‘objective’. It is most meaningful to assume a continuum that runs from purely subjective to purely objective. Completely arbitrary estimates of probability and harm are purely subjective; purely objective, on the other hand, are the estimates of probability and harm made from an Archimedean point (a ‘god’s eye view'). Understood like this, risk calculations are rarely either purely objective or purely subjective. We come closest to the purely objective pole when harm or benefit are given and probability can be calculated mathematically. It must be emphasised that this strong form of objectivity is not identical to what natural sciences refer to as 'objective risk'. Scientific risk assessments are based on empirically established figures and statistical probabilities, which are, at best, an approximation of what we mean here by 'pure objectivity'. If we consider the risks of synthetic nanoparticles in this context, it is clear that they should currently be classified as the third type of uncertainty. This does not mean that an assessment of the associated risks is subjective in the sense of arbitrary. We are not forced to construct purely hypothetical scenarios; but at the same time we do not have sufficient knowledge to evaluate the risks with scientific 'objectivity' either. In this situation, empirical and circumstantial evidence is available to indicate that synthetic nanoparticles can be dangerous to human health and the environment. But this evidence is so full of gaps that we cannot yet calculate the risks with the required reliability (as is the case in the authorisation of new medicines), although this example also shows that reliability does not mean infallibility or absolute safety.

So far there has been consensus that the precautionary principle should be applied only in a situation of uncertainty. There is, however, less agreement on whether the principle should apply to all potential harm or only particular types, i.e. irreversible and severe. Below, I assume the latter. This means that the precautionary principle does not require a generalised attitude of risk aversion. It is intended only for particular cases, for certain kinds of unfamiliar risks: where there is scientific uncertainty and substantial or severe harm is imminent. In such situations, and only in such situations, the precautionary principle requires the State to take appropriate precautionary measures in order to prevent this harm taking place.

After clarifying what is meant by uncertainty, the next question is what we mean by severe and irreversible harm. No definitive answer can be given here. Suffice it to say that the word 'harm' has both descriptive and evaluative or normative meanings. We can describe harm; and this also means we can determine whether harm has occurred or not. Seen evaluatively, harm is relative to a positive reference point: a state of a person, object or system (e.g. a company or an ecosystem), which is desirable and therefore worthy of protection, which is changed in a negative sense in the event of harm. In this sense harm would be a negative divergence, which should be avoided, from a desirable (and thus worth protecting) state. The central question is then: which states or goods are desirable and worth protecting? And how can we determine the magnitude of harm? These questions would require a detailed engagement with the issue of whether harm can be determined objectively, i.e. independent of desires and convictions, or only subjectively, i.e. only in relation to desires and convictions; and whether there are objective values that provide a gauge with which we can determine harm and its extent. I will leave these questions open here. This much is, however, undisputed: in a relatively large number of cases we are in agreement over what harm would be, and we are often in agreement about its extent as well. We agree that the adverse effects of a technological product on (human) health – whatever health is – constitutes harm. And depending on the impact, it may be slight, significant or severe harm to health, where the most severe harm to a person's health is death. In terms of environmental harm the criteria are perhaps less clear, but here too there is relatively extensive agreement on the nature of harm and its extent. No more is necessary in our present context. We can say with good conscience that the potential harm of synthetic nanoparticles to health and the environment is, in the worst case, severe if not catastrophic.

To summarise, let me emphasise once more that the precautionary principle is not based solely on the assumption that severe and irreversible harm is imminent. It is equally important that the probability of harm occurring cannot be calculated precisely, neither scientifically (statistically) nor on the basis of general knowledge, although first indications and evidence are available so that relatively unspecific statements about probabilities can be made. Only when both conditions are fulfilled can the precautionary principle be applied. Its core thesis is then that if there are empirical indications of potentially severe harm and certain careful and interim assumptions about the probability of occurrences seem plausible, risk-averse behaviour is not only sensible but ethically required. But what is 'risk-averse behaviour'?

In the literature, many seem to be of the opinion that it is tantamount to a type of maximin (Sandin 2007:102f.). From the standpoint of 'the prevalence of the bad prognosis', in situations of uncertainty we should always decide so as to avoid the greatest possible harm – independently of its probability of occurrence, and also independently of the potential benefit. This disregard of probability and benefit may be defensible in disaster scenarios, in particular those affecting a large number of people like a Maximum Credible Accident (MCA) in a nuclear power station. But as the example of synthetic nanoparticles shows, equating the precautionary principle with the maximin criterion is inadequate if we assume potentially severe but not catastrophic harm, and different (assumed) probabilities of occurrence according to the kind of exposure.

5. Caution in handling synthetic nanoparticles

It has become common to distinguish between weak and strong readings of the precautionary principle (Rippe 2002). Both relate to potentially severe harm, the probability of which cannot yet be determined with scientific reliability (even if there are empirical indications of the type of harm that might occur, and its likeliness of occurring). The precautionary measures they suggest, however, differ in their extent.

The strong reading emphasises three points:

A) *Reversal of burden of proof.* It is not the State, but the proponent (producer) of a hazardous technology who must prove that it is harmless (for example, drugs or food additives).

B) *Emphasis on the limits of knowledge.* The principle of complete scientific proof is rejected. Ecological and biological connections are too complex to explain completely using scientific means.

C) *If in doubt, refrain*. Any activity that could produce severe and long-term harm to the environment or humans should be prohibited.

The weak reading differs here in the following ways:

A) *Maintain burden of proof.* In accordance with the general rule of 'innocent until proven guilty', the State may intervene to regulate only if it can prove the danger of a technology or a product.

B) *Perform a careful risk analysis.* The aim of the analysis is to determine the risks of a technology – the probability and magnitude of harm – scientifically.

C) *Take precautions, but act*. A technology may be developed even in the absence of scientific proof that it is harmless. However, the State does have the right, and even the duty, to impose precautionary measures on the proponents in order to minimise the risks.

Whether the strong or the weak precautionary principle is applicable to an ethically responsible approach to the risks of synthetic nanoparticles depends largely on how those affected will be exposed. Four groups can be distinguished: 1) Researchers; 2) Employees of plants that manufacture synthetic nanoparticles or use them in large quantities; 3) Uninvolved third parties, particularly consumers (in medical cases these are patients) of products that contain unbound synthetic nanoparticles; 4) The environment (water, air, soil, groundwater etc.).

1) Researchers

Since we cannot make general statements about the toxicity of synthetic nanoparticles, it is sensible to start from an example where there is already evidence of a risk potential. There is support for the idea that free and uncoated nanotubes, especially in aggregated form, may pose a significant risk to human health. Let us also assume that uninvolved third parties are not affected, but only people directly involved in research. This means that it is reasonable or prudent and thus in their interest to take the necessary precautionary measures. Obliging the researchers to do so would however not be justified, if they make an autonomous, i.e. voluntary and fully informed decision to expose themselves to the risk in question. For in terms of autonomy, we can choose to expose ourselves to any kind of risk, as long as we have been informed about it and no danger is presented to uninvolved third parties. At the same time we should not assume that the researchers view themselves as guinea pigs. They themselves should take care to protect themselves as far as they can from possible danger, for example, by using hermetically sealed systems. These precautionary *measures* have nothing to do with the precautionary *principle*, as they involve minimising the researcher's own risks.

However, these measures must, as far as possible, prevent uninvolved third parties (outside the research laboratories) from coming into contact with the synthetic nanoparticles used for research purposes and thereby being exposed to a health risk. Here, the precautionary principle comes into play. If, in the worst case, only small quantities can escape and the probability of severe harm can therefore be assumed to be extremely small, the weak precautionary principle is appropriate: research and development should take place, but measures should be taken to ensure that the risk to uninvolved third parties is minimal.

2) Employees

How should we evaluate, in ethical terms, the situation of employees in companies that produce synthetic nanoparticles in large quantities, or use them in the manufacture of other products?[16] Here we cannot assume they have made a voluntary and informed decision.[17] In addition, with the current state of knowledge in occupational medicine and toxicology, and while there are no standardised measuring procedures available, no threshold values can be justified. Therefore, mass production or mass use is only permissible if employees are exposed to no or extremely minimal health risk. Whether this is the case at present is questionable. Above all, it is unclear whether the standard procedures for limiting exposure – including technical protective measures such as the use of closed apparatus, organisational measures such as minimising duration of exposure, and person-related protective measures such as the use of protective clothing and respiratory filters (Suva 2006) – are sufficient to exclude severe harm to health. There are also questions about whether filters at the current

[16] 'Thousands of tons of silica, alumina and ceria, in the form of ultrafine abrasive particle mixtures that include nanoparticles, are used each year in slurries for precision polishing of silicon wafers. (…) The manufacture of fullerenes could soon match the engineered metal oxide nanoparticles in production quantities, with the Kitakyushu plant (Mitsubishi, Japan) estimating an annual production of 1500 tons of C_{60} by 2007. Other manufacturing facilities also anticipate increased production of fullerenes, and therefore the sum production could be several thousands of tons of fullerenes by 2007. (…) The worldwide production capacity for single-wall and multi-wall carbon nanotubes is estimated to be about 100 tons in 2004, increasing to about 500 tons in 2008 (…) Although current production of engineered nanomaterials is small, it is evident that production rates will accelerate exponentially in the next few years' (Borm *et al.* 2006).

[17] The objection could be raised that the employees of the company, as long as it is not acting quite irresponsibly, will be informed of the possible risks of their work. In addition, nobody is forced to work in a factory that makes synthetic nanoparticles. In this case, therefore, it is assumed that decisions are voluntary and informed. This objection holds as long as 1) every employee has a genuine (not just theoretical) possibility of changing workplace if he/she considers the risks to be too great; and 2) if he/she really has been informed about the risks in an unbiased and comprehensive way. It appears to me that it is unrealistic to assume that these conditions will always be fulfilled. The voluntary and informed nature of the choice cannot thus simply be taken as given.

state of technology can indeed provide adequate protection.[18] If these concerns are justified, there is much in favour of applying the strong precautionary principle, in particular point C: Given the prevalence of the bad prognosis, the mass production and mass use of synthetic nanoparticles such as nanotubes should currently be prohibited on the grounds that they could cause severe harm to the employees, even if there are indications that the probability of such harm is small, and that the potential benefits of synthetic nanoparticles are great. Currently means that the prohibition could be lifted if a) risk research shows that the potential harm of these nanoparticles is smaller than suspected; or b) if it can be guaranteed that employees are exposed to no health risk, or only a very small one. Furthermore, it must be ensured that under normal conditions, significant quantities of such nanoparticles cannot enter the environment, i.e. into water, air, soil or groundwater.[19]

3) Uninvolved third parties

The issue of the industrial production of synthetic nanoparticles is one thing; whether such particles may be used in products, and if so in what form, is quite another. As already indicated, the use of unbound synthetic nanoparticles is particularly problematic. Here, the question is how the burden of proof should be distributed: should point A of the weak precautionary principle be maintained? Or is a reversal of burden of proof necessary, as point A of the strong precautionary principle claims? In view of the potential risk from certain synthetic nanoparticles, and based on the existing scientific evidence, it appears that the reversal of proof required by the strong precautionary principle is justified. This applies at least to products containing unbound synthetic nanoparticles, for example all products that use delivery technology and therefore such synthetic nanoparticles as fullerenes, dendrimeres or gold nanoparticles. Such products – particularly in the fields of nanomedicine, nanopesticides and nanofood – require authorisation from an ethical standpoint. The producer must use specific test procedures, monitored by the appropriate authorities, to prove these products are harmless. The nanoproducts in question should thus be treated like medicines.

To reiterate, however, this does not mean that absolute proof of safety is required. The criteria to be fulfilled in order to provide proof would have to be determined for nanoproducts specifically. Rules at different levels of strictness are imaginable. Even after authorisation, there would in addition have to be monitoring to detect any long-term effects. It is clear that this approach requires functioning patent protection, and would also make the products in question relatively expensive. Such economic considerations would nevertheless have to take a back seat to the ethical considerations mentioned above.

The synthetic nanoparticles used in existing products are generally integrated into a vehicle – such as the nanotubes in tennis rackets. They are thus insulated from the

[18] 'Face masks offer only slight protection in this case. Only a comprehensive plant air-filtering system could remove the particles, an extremely costly and, indeed, hardly realisable solution, given the current offer of air-purification systems for large buildings. … Presumably, nanoparticles must be handled with the same care given certain bio-organisms or radioactive substances. Adequate protection measures, such as a nano-compatible "glove box", will probably have to be developed to ward off possible dangers' (Swiss Re 2004:33f.).

[19] According to Oberdörster, the following possibilities currently exist for unbound nanoparticles to enter the environment: 1) 'Some [manufactured nanomaterials] are and others will be produced by the ton, and some of any material produced in such mass quantities is likely to reach the environment from manufacturing effluent or from spillage during shipping and handling'. 2) 'They are being used in personal-care products such as cosmetics and sunscreens and can therefore enter the environment on a continual basis from washing off of consumer products'. 3) 'They are being used in electronics, tyres, fuel cells, and many other products, and it is unknown whether some of these materials may leak out or be worn off over the period of use'. 4) 'They are also being used in disposable materials such as filters and electronics and may therefore reach the environment through landfills and other methods of disposal'. [These materials also include food packagings that contain nanoparticles.] 5) 'Scientists have also found ways of using nanomaterials in remediation. Although many of these are still in testing stages (…) dozens of sites have already been injected with various nanomaterials, including nano-iron' (Oberdörster *et al.* 2005:825).

environment and not associated with the same risks as the unbound form. Of course, this is only the case as long as they really are anchored into a matrix. Here, the following questions must be answered: 'What happens to the nanocomponents when the devices and materials are disposed of? There are no plans for recycling or reuse as yet. Should it be possible that these nanoapplications decompose at the end of their lifecycle' (Boeing 2005:36), the bound synthetic nanoparticles would be released and thus become a risk to humans and the environment. This is an important reason for pressing ahead with research into the lifecycles of the products in question.

Products containing bound synthetic nanoparticles that are already available should however not be taken off the market, as the quantity of the particles is certainly too small to cause significant harm in the event of their release. (Or to put it another way, the risk – i.e. the probability of such harm – is so small as to be acceptable.) Nevertheless, these articles should require notification. And producers should be required to provide a clear concept for disposal, showing how the products are recycled and what then happens to the synthetic nanoparticles.[20] The weak precautionary principle is applicable in this area. Existing nanoproducts may continue to be manufactured and sold if the required quantities of nanoparticles are present, but only under particular conditions; they require notification, and careful risk and lifecycle analyses must be performed, especially regarding their disposal, in order to ensure that the smallest possible quantity of unbound synthetic nanoparticles is released. In addition, a duty of declaration should apply to all (commercial) products containing synthetic nanoparticles. There are two reasons in favour of such an obligation. For one thing, in this case there is a duty to inform consumers, and for another, a declaration is a measure that helps foster trust.

4) The environment

The release of synthetic nanoparticles into the environment to detoxify contaminated soils and polluted groundwater should be discontinued until further notice. Points A and C of the strong precautionary principle are critical here: such a release, especially of large quantities, could cause severe harm to animals, plants and whole ecosystems. The rule that therefore applies here is to refrain where uncertainty remains ('if in doubt, refrain').[21] This would change only if it could be scientifically demonstrated that no severe harm is imminent[22] or that it could be prevented, and that the release can indeed achieve its intended goal.[23]

Synthetic nanoparticles can also enter the environment by being washed out of cosmetics or clothes; or if they are used directly as unbound nanoparticles, in products such as washing machines. One example that has caused major controversy in America is nanosilver (Weiss 2006). In late 2006 the American Environmental Protection Agency (EPA) adopted the resolution that manufacturers of products containing (unbound) nanosilver particles must provide proof that these particles do not pose any risk either to humans or, especially, to the

---

[20] They should at least participate in the necessary research. This is important and justified, for the following reason: 'Effluent from nanomanufacturing processes, use of nanoparticle-containing substances such as sunscreens, and disposal of nanomaterial-containing products, will inevitably lead to increasing quantities of engineered nanomaterials in water systems. If we cannot track these materials, it will be almost impossible to determine how benign or harmful their presence is. The (…) challenge therefore is to develop instruments that can track the release, concentration and transformation of engineered nanomaterials in water systems (including liquid-based nanotechnology consumer products), within the next five years' (Maynard *et al.* 2006).

[21] 'Uncertainty' is important, because we do not know whether severe harm would really occur. There are only indications that it could do so, although estimating the probability is particularly difficult in this case because of the uncertainty. The thesis is that these indications are sufficient to justify a temporary prohibition.

[22] This means that the probability of such harm is so small that the risk – the product of probability and harm or extent of harm – can be viewed as acceptable.

[23] In this discussion, point B of the strong precautionary principle plays no role. All are in agreement that the extent of harm and the probability of occurrence could in principle be determined, even in terms of the impact of nanoparticles on ecosystems, although this is not possible at present.

environment. This rule affects a whole range of products, from air fresheners to plastic containers for storing foods, to special shoe inlays. The EPA is particularly concerned about a washing machine from Samsung, in which unbound silver nanoparticles are used to make laundry germ-free(er) without having to use hot water or bleaching agents. The nanosilver particles used in these products have an antimicrobial effect.[24] They are able to destroy bacteria and other microorganisms. If they enter the environment as unbound particles there is a risk that they will destroy useful bacteria and aquatic organisms. Products that claim to kill germs based on their use of nanosilver are viewed by the EPA as pesticides, i.e. products with pesticidal components that therefore require authorisation.

This appears to be the first time that an authority has applied the strong precautionary principle, in particular point A, i.e. reversal of the burden of proof, to synthetic nanoparticles. Is reversing the burden of proof really justified in this case? The answer is yes. If large quantities of free nanosilver particles enter the environment, there is a danger that these particles will kill useful bacteria and aquatic organisms and thus cause substantial harm. It is understood that we are talking about a suspicion, and not a scientifically founded certainty. But this suspicion is not purely hypothetical. It has an empirical basis: knowledge of the antibacterial effect of silver. Therefore the requirement to reverse the burden of proof is justified.

In summary, one can say that from an ethical point of view, the handling of synthetic nanoparticles should be regulated internationally as uniformly as possible. This regulation should be in accordance with the precautionary principle. This would have two effects. First, there would be an intensification in risk research, taking the necessary safety measures into consideration. Second, there would presumably also be a deceleration in the development and marketing of new commercial products containing synthetic nanoparticles in unbound form. This does not mean that nanotechnology will be unjustifiably disadvantaged in relation to other technologies. What we are talking about is responding to the risks of this technology in an appropriate way. The decisive point in this context is that if there are reasonable grounds for thinking that, under particular conditions, synthetic nanoparticles can severely harm humans and the environment, then it is justified to reverse the burden of proof and require manufacturers to prove that the (free) nanoparticles used in their products are harmless.

Bibliography

Bachmann Andreas, David Badri, Esther Brunner, Reto Cueni, Alessandro Danieli, Patrick P. Eberhard, Gerald Hess, Laurent Lerf, Benjamin Rath, Klaus Peter Rippe, Bernhard Rom, Tamara Rüegger, Nora Schmid, Thomas Schmidt, Annette Schulz-Baldes, Dominik Tasnady, Ariane Willemsen (2006), 'Elemente der Risikoethik', http://www.ethikdiskurs.ch/umweltethik/Elemente_Risikoethikpdf.pdf.

Boeing, Niels (2005), 'Unsichtbare Gefahr', in: *Technology Review* 11, November 2005, pp. 32–42.

Borm, Paul JA, David Robbins, Stephan Haubold, Thomas Kuhlbusch, Heinz Fissan, Ken Donaldson, Roel Schins, Vicki Stone, Wolfgang Kreyling, Jürgen Lademann, Jean Krutmann, David Wahrheit, Eva Oberdörster (2006), The Potential Risks of

[24] It has been known for thousands of years that silver has antiseptic properties. This effect is further increased in nanosilver. Nanoscale silver is playing an increasingly significant role in preventing infections, because of its antibacterial properties, for example in wound treatment and in general hospital hygiene (nanosilver-coated surgical instruments and catheters).

Nanomaterials: a Review carried out for ECETOC, http://www.particleandfibretoxicology.com/content/3/1/11.
Bottini, Massimo, Shane Bruckner, Konstantina Nika, Nunzio Bottini, Stefano Bellucci, Andrea Magrini, Antonio Bergamaschi, Tomas Mustelin (2006), 'Multi-walled carbon nanotubes induce T lymphocyte apoptosis', in: *Toxicology Letters* 160, pp. 121–126.
Brune, H., H. Ernst, A. Grunwald, W. Grünwald, H. Hofmann, H. Krug, P. Janich, M. Mayor, W. Rathgeber, G. Schmid, U. Simon, V. Vogel, D. Wyrwa (2006), *Nanotechnology. Assessment and Perspectives,* Berlin/Heidelberg.
Brunner, Tobias J., Peter Wick, Pius Manser, Philipp Spohn, Robert N. Grass, Ludwig K. Limbach, Arie Bruinink, Wendelin J. Stark (2006), 'In Vitro Cytotoxicity of Oxide Nanoparticles: Comparison to Asbestos, Silica, and the Effect of Particle Solubility', in: *Environmental Science & Technology* 40/14, pp. 4374–4381.
Chen, Zhen, Huan Meng, Genmei Xing, Chunying Chen, Yuliang Zhao, Guang Jia, Tiancheng Wang, Hui Yuan, Chang Ye, Feng Zhao, Zhifang Chai, Chuanfeng Zhu, Xiaohong Fang, Baocheng Ma, Lijun Wan (2006), 'Acute toxicological effects of copper nanoparticles in vivo', in: *Toxicology Letters* 163, pp. 109–120.
EMPA-News 2/2006, http://www.empa.ch/plugin/template/empa/1030/48763/---/l=1.
Hansson, Sven Ove (2007), "Risk", in: *Stanford Encyclopedia of Philosophy*, http://plato.stanford.edu/entries/risk/.
Limbach, Ludwig K., Peter Wick, Pius Manser, Robert N. Grass, Arie Bruinink, Wendelin J. Stark (2007), 'Exposure of Engineered Nanoparticles to Human Lung Epithelial Cells: Influence of Chemical Composition and Catalytic Activity on Oxidative Stress', in: *Environmental Science & Technology* 41/11, pp. 4158–4163.
Locatelli, Sandrine, Carole Nicollet, Jean Charles Guibert, Manuela Denis (2005), 'Potential Risks of Nanotechnologies', Part 3 of the 4th Nanoforum Report, www.nanoforum.org.
Long, Thomas C., Navid Saleh, Robert T. Tilton, Gregory V. Lowry, Bellina Veronesi (2006) 'Titanium Dioxide (P25) Produces Reactive Oxygen Species in Immortalized Brain Microglia (BV2): Implications for Nanoparticle Neurotoxicity', in: *Environmental Science & Technology* 40/14, pp. 4346–4352.
Maynard, Andrew D., Robert J. Aitken, Tilman Butz, Vicki Colvin, Ken Donaldson, Günter Oberdörster, Martin A. Philbert, John Ryan, Anthony Seaton, Vicki Stone, Sally S. Tinkle, Lang Tran, Nigel J. Walker, David B. Wahrheit (2006), 'Safe handling of nanotechnology', in: *Nature* 444, pp. 267–269.
Oberdörster, Günter, Eva Oberdörster, Jan Oberdörster (2005), 'Nanotechnology: An Emerging Discipline Evolving from Studies of Ultrafine Particles', in: *Environmental Health Perspectives* 113/7, pp. 823–839.
Oberdörster, Eva (2004), 'Manufactured nanomaterials (fullerenes, C60) induce oxidative stress in the brain of juvenile largemouth bass', in: *Environ. Health Perspect.* 102, pp. 1058–1062.
Renn, Ortwin, Mike Roco (2006), White Paper on Nanotechnology Risk Governance, http://www.irgc.org/irgc/_b/contentFiles/IRGC_white_ paper_2_PDF_final_version.pdf.
Rippe, Klaus Peter (2002), 'Vorsorge als umweltethisches Leitprinzip', http://www.ethikdiskurs.ch/umweltethik/Vorsorgeprinzip.pdf.
Rippe, Klaus Peter (2006) 'Ein Vorrang der schlechten Prognose? Zu den ethischen Grundlagen des Vorsorgeprinzips', in: *Neue Zürcher Zeitung*, 30 December 2006.
Sandin, Per (2007), 'Common-Sense Precaution and Varieties of the Precautionary Principle', in: Tim Lewens (ed.), *Risk. Philosophical Perspectives*, London/New York, pp. 99–112.
Schulte, Paul A., Fabio Salamanca-Buentello (2007), 'Ethical and Scientific Issues of Nanotechnology in the Workplace', in: *Environmental Health Perspectives* 115/1, pp. 5–12 (accessible on the Internet at http://www.ehponline.org/members/2006/9456/9456.pdf.).

Scientific Committee on Emerging and Newly Identified Health Risks SCENIHR (2007), ‘Opinion on the Appropriateness of the Risk Assessment Methodology in accordance with the technical Guidance Documents for new and existing Substances for assessing the Risks of Nanomaterials’, http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_004c.pdf.

Shelley, Toby (2006), *Nanotechnology. New promises, new dangers*, London, New York.

Sunstein, Cass R. (2007), *Gesetze der Angst. Jenseits des Vorsorgeprinzips*, FfM.

Suva (2006), ‘Nanopartikel an Arbeitsplätzen’, http://www.suva.ch/nanopartikel_an_arbeitsplaetzen.pdf.

Swiss Re (2004), *Nanotechnology. Small matter, many unknowns*, http://www.swissre.com.

Tiefenauer, Louis (2007), ‘Magnetic Nanoparticles as Contrast Agents for Medical Diagnosis’, in: Tuan Vo-Dinh (ed.), *Nanotechnology in biology and medicine: methods devices, and applications,* Boca Raton, FL.

Weiss, Rick (2006), ‘EPA to regulate Nanoproducts sold as germ-killing’, in: *The Washington Post*, 23 November 2006.

Yang, Ling, Daniel J. Watts (2005), ‘Particle surface characteristics may play an important role in phytotoxicity of alumina nanoparticles’, in: *Toxicology Letters* 158, pp. 122–132.