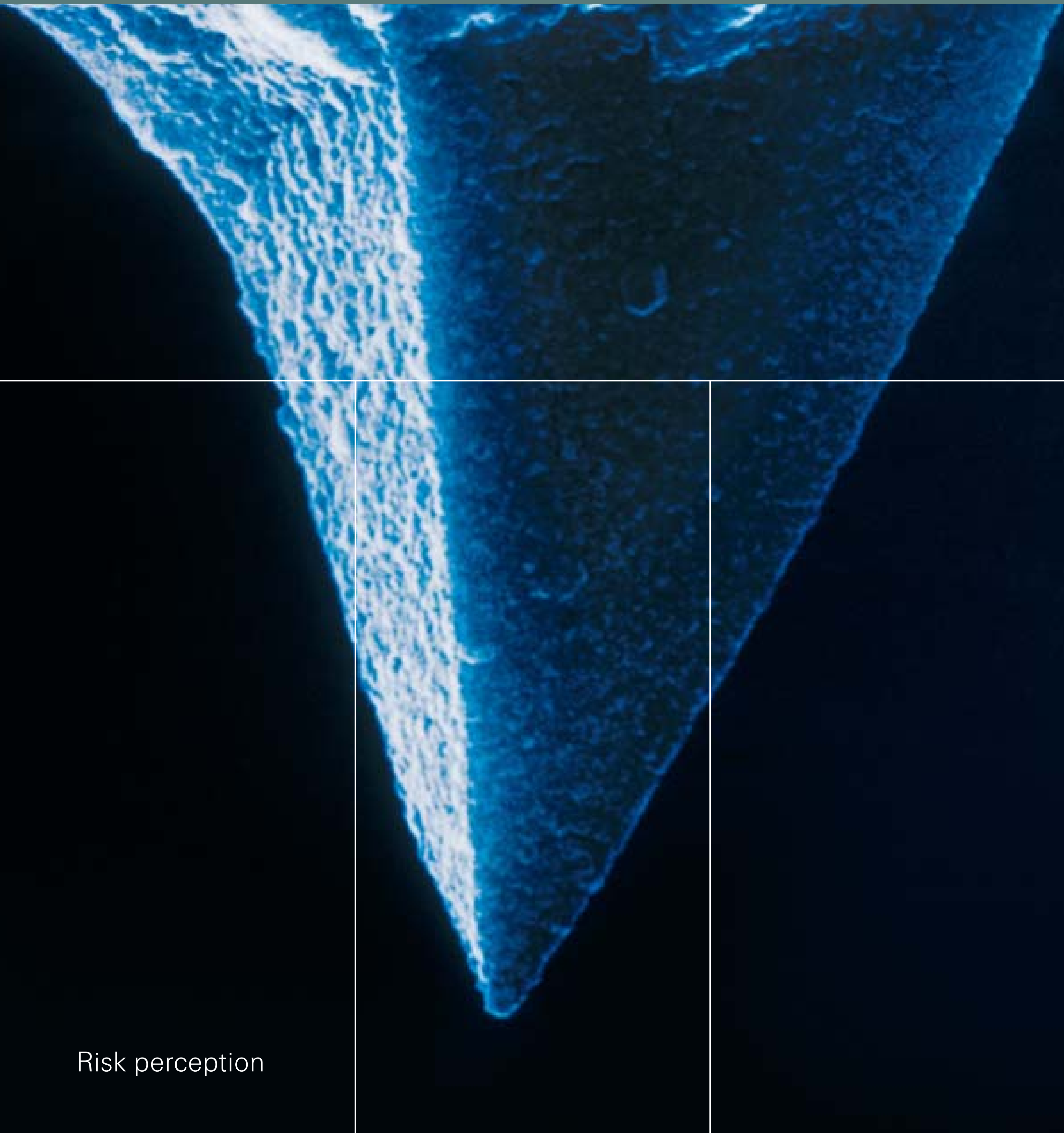
Swiss Re

Nanotechnology
Small matter, many unknowns



Risk perception

Nanotechnology
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Preface

Nanotechnology is a major new approach in industrial production and reflects the general downscaling and miniaturisation efforts prevalent in all technological disciplines. It allows structures and tailor-made particles a few millionths of a millimetre in size to be manufactured in a controlled manner and is used to produce, for example, faster computer chips, more efficient batteries, "carriers" for medicines or ultra-thin coatings with multiple properties.

Until recently, the phrase that "technology cuts both ways" was rarely associated with nanotechnology. However, its commercial utilisation has triggered controversy in specialist circles, and the term itself is rapidly becoming a buzzword in the media and the public at large. Questions abound regarding the opportunities and – from an insurance perspective – the hazards of nanotechnology. Are the invisible particles emitted by air fresheners dangerous to our breathing? What happens when products manufactured using nanotechnology end up on waste disposal sites and their particles are released into the environment? Can nanoparticles in suntan lotions find their way into the body via the skin and produce harmful effects? To date, not enough is known about the implications of this novel discipline, and the paucity of data in this field invites a host of fears and alarmist scenarios.

Since the use of nanotechnology in commercial production is set to spread rapidly, the insurance industry should waste no time in assessing the potential risks and benefits both for itself and for society in general. Swiss Re has dedicated teams of experts which track new or emerging risks, and nanotechnology is one of the topics currently in focus. After all, it is vital for the insurance industry to know what losses a new technology can give rise to and what the extent and frequency of such losses will be. Once these basics have been roughly established, insurers will be in a better position to assess the future loss burden, calculate a premium commensurate with the risk and grant adequate insurance cover.

Considering the many benefits of nanotechnology, Swiss Re is working towards a transparent risk dialogue with the various stakeholders – industry, scientists, regulators and the insurance sector alike – to discuss its inherent risks and opportunities. Rather than limit itself to the study of individual risks associated with nanoparticles, the insurance industry must endeavour to assess the general risk represented by nanotechnology as a whole. Once it is in the position to evaluate this risk, the insurance industry will be able to define what it considers a claim and decide how to handle it optimally.

Bruno Porro
Chief Risk Officer, Swiss Re

Fullerene C60 molecules at a resolution of 10 nm.
With the aid of the scanning tunneling microscope (STM) molecules can be stimulated to emit light in a vacuum.

1 Introduction

The term "nanotechnology" is derived from the Greek word "nanos", meaning "dwarf". A nanometre is one thousand millionth of a metre or, in other words, one millimetre equals a million nanometres. Measurements of this scale are hard to imagine. For comparison purposes, the size of a red blood corpuscle is approximately 7,000 nm. Bacteria are even smaller, measuring about 1,000 nm, whereas a ball-shaped virus measures some 60–100 nm. A flea, on the other hand, at 1 million nm is close to gigantic!

Nanotechnology is the subject of the latest technology debate to impinge on the public consciousness. The word itself actually connotes less a technology than a generic term for a large number of applications and products which contain unimaginably small particles and demonstrate special properties as a result. Nanoparticles are too small to be visible to the naked eye – so small, in fact, that one would have to split a human hair 80,000 times before it reached a width of 1 nanometre.

The tendency to reduce the size of products is nothing new. Many everyday objects, such as the portable computer or the mobile phone, have been constantly reduced in size as successive technological advances made that possible. Despite downsizing, the properties of the products have been retained and even greatly improved in most cases. The first mainframe computers of the early 1950s, one recalls, could only perform simple calculations. Today, we work on PCs that fit conveniently onto a desk and perform tasks much more complex than purely computing operations and at record speed. Although computers can now be used to view or process images and even listen to music, their basic function still remains the same: namely, that of digitised data processing.

The fundamental contrast to nanotechnology is that in this new discipline, the downsizing process has broken through a certain barrier; beyond it, the old laws no longer necessarily apply. Any material reduced to the size of nanoparticles can suddenly behave much differently than it did before. Electrically insulating substances, for example, suddenly become conductive, and insoluble substances, soluble. Others change colour or become transparent – demonstrating completely new properties that open the door to novel applications and products, thus making them of great interest both to industry and society at large.

The range of new products is wide. From self-cleaning window panes, drinking glasses or aeroplane seats to tailormade drugs, cosmetics, packaging materials, food additives, electronic products or household goods, everything is conceivable – and many of these are already on the market. The drivers include many of the "Fortune 500" companies, which have joined numerous smaller companies and research institutes in the race for new market segments and patents. Yet, nanotechnologically manufactured products have been retailed for some time now without any particular labelling by regulators and have thus not been recognised by consumers for what they are.

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"Every nation in the world is looking at nanotechnology as a future technology that will drive its competitive position in the world economy."
Neal Lane, Professor of Physics, Rice University [1]

An industrial revolution?
Some experts consider the emergence of nanotechnology to be an industrial revolution that – much like the invention of electricity – will have an enormous impact on society, the economy and life in general. In this respect, nanotechnology follows biology and information technology, while the boundaries among them grow ever more fluid and the disciplines mutually complement one another. At the nuclear level, the laws of physics, chemistry and biology merge, facilitating interdisciplinary developments that are expected to outweigh all previous achievements. These changes affect just about every conceivable branch of industry: aerospace technology, car manufacturing, chemicals, medicine, electronics, computer technology, optical instruments, mechanical engineering and precision mechanics.

Following e-business, nanotechnology is already being hailed by industry as the next "quantum leap" and its opportunities and potential lauded. The degree of attention being paid to this technology is reflected in the rapid increase in research funding by industry and governments. According to estimates for the year 2003, public research funding alone totalled more than USD 3 billion worldwide and was still increasing. It is generally assumed that industry in the same period invested at least the same amount. Sales revenues from products manufactured using nanotechnology have already reached eleven-digit figures and are projected to generate twelve-digit sums by 2010, even thirteen-digit sums by 2015. And this tearaway development reflects a trend affecting all nations in the industrialised world in equal measure.

Nanotechnology was used years ago in some manufacturing techniques, yet industrialists were not really aware of it as such. When the first tyres were made with carbon black in the 1920s to reduce abrasion by the road surface, no one realised that the improved tyre quality was due to the enclosed ultra-small particles. At that time, manufacturing particles of a fixed size was not yet possible, nor were the causal connections fully understood. Today's systematic use and manipulation of individual nanoparticles was only realised through the invention of special tools, such as the scanning tunnel microscope (STM) and the atomic force microscope (AFM), and their improved versions in the 1980s. It was only through the advances in visualisation and the possibilities of systematic manipulation that the broad potential of this technology became clear, leading to its increased use in manufacturing in recent years.

A number of new products were launched on the market following a relatively short phase of research and development. To effectively determine both the long-term properties and the general reliability of these products and their effects on consumers and the environment, all the involved parties must endeavour now to gather experience and analyse data, Clearly, this must be done since – as in any other new technological development – specialist circles and society at large have neither solid knowledge derived from the past nor a suitable method for definitively assessing the consequences of any changes that may arise in the future.

1 Ann Thayer, "Nanotech meets market realities," *Chemical & Engineering News* (2002): p. 17.

"There is no doubt that this science of the vanishingly small is the beginning of something very big indeed. But how far can it go? How fast? What are the societal, environmental, health and business implications?"
Simon Waddington, Advisory Board of the European Nanobusiness Association (ENA)[2]

The miniaturisation of material down to nanoparticle size yields a host of surprises: not only can the behaviour of small particles be changed, but so, too, can their mobility. In contrast to larger microparticles, nanoparticles have almost unrestricted access to the human body. The possibility of absorption through the skin is currently under discussion, while the entry of certain nanoparticles into the bloodstream by inhalation via the lungs is considered a certainty. Some of the tiny particles can also get into the body via the digestive tract. Once in the bloodstream, they move practically unhindered throughout the entire body. Even obstacles as hard to overcome as the blood-brain barrier (see page 23) seem to present no major problem to some nanoparticles. According to laboratory reports, test particles previously administered can be detected in the brain even after a short period.

Coated nanoparticles can be extremely mobile in the environment. Once airborne, they can drift on more or less endlessly, since they – unlike larger particles – do not settle on surfaces, but are only stopped when, for example, they are inhaled or their dissemination is limited in some other way. On land, in the earth and in the water, the same holds true. The smallest particles are washed through various earth strata and spread unhindered in a liquid medium, which means they pass easily through most filtering methods currently in use. In the normal processing of drinking water, for example, nanoparticles would not be filtered out completely.

Now, the mere presence of the particles, even if they appear to be ubiquitous, is not in itself a threat. Only if certain properties of the particles should prove harmful to human beings or the environment could one point to a genuine hazard. Whether – and to what extent – nanoparticles or products manufactured with them constitute a specific hazard is hard to determine in the absence of specially funded studies, and hardly any long-term or toxicological studies are currently available.

Yet questions are already being raised. How will the changed chemical properties of the nanoparticles affect the body if they are used in concentrated form, such as in drugs or sprays? What happens to the accumulated particles that have already been detected in some organs? How many of them are excreted and via what channels?

For human beings, the range of products and applications made possible by nanotechnology is something fundamentally new. Man has never really had to cope with this kind and quantity of industrially manufactured particles. Are we sufficiently prepared for the large-scale introduction of this technology?

Finding a satisfactory answer to this question is expected to take some time. While some limited conclusions may be drawn from scientific experiments on cells and animals, definitive results from these activities will likely remain outstanding. As in all medical research, the results of animal experiments cannot be applied to human beings without qualification. In order to find out how nanoparticles behave in the human body, studies would have to be carried out on test persons, and at this stage, that is an unrealistic prospect. Potential hazards to humans and the environment resulting from the introduction of nanotechnology cannot be entirely excluded. In view of this latent uncertainty and in keeping with the precautionary principle, the most obvious protective measures must be taken alongside a continuing programme of risk analysis.

2 *Venture Capital Magazine* (November 2002): p. 4.

1 Introduction

As one of the major risk bearers, the insurance industry can only responsibly support the introduction of a new technology if it can evaluate and calculate the risks associated with it. Given the heterogeneity and global dissemination of nanotechnologically manufactured products, and the fact that they are being sold – and are generally covered by existing treaties in insurance already – this is no easy task.

As with every new technology, the opportunities and the risks have to be weighed. Undeniably, nanotechnology makes possible a large number of innovative products that may be attractive to consumers and beneficial to the environment alike. The trend towards miniaturisation also carries within it a potential for growth, which analysts say will be of greater economic significance in the years to come. It is therefore important to take a critical view of nanotechnology in order to find out where – if at all – possible problems may arise.

"Nanotechnology has given us the tools (...) to play with the ultimate toy box of nature – atoms and molecules. Everything is made from it (...) The possibilites to create new things appear limitless."
Horst Störmer, Nobel Laureate, Physics, 1998 [3]

Advanced nanotechnology
The political arena has seen controversial debate for some time now on the risks associated with nanotechnology. Surprisingly, attention has been riveted on what is called "advanced nanotechnology", the area of nanotechnology dealing with Artificial Intelligence, nano-robots and "self-assembly" (self-organisation).

We are, however, still a long way from this type of nanotechnological self-assembly. Whereas optimists maintain that this mode of production is basically possible, pessimists believe that the technology will not be available to the next few generations should it ever prove to be feasible. Although these scenarios may only evolve in the distant future, they have been preying on people's imagination for some time, giving rise to horrific visions of intelligent, self-reproducing particles which might swarm all over the world and make it uninhabitable for humans. Visions of "grey goo" such as these have triggered many of the debates conducted in social and political forums.

Interestingly, nanotechnological risks are often associated with objects capable of independent action, an idea which still belongs in the realm of science fiction. The potential hazards relating to the manufacture of real and innovative materials or new applications, however, have attracted little attention. The insurance industry is mainly interested in those products already commercially available or just short of market launch. For this reason, the publication in hand concentrates on the field of nanoparticle manufacture and materials development. This may be a limited field, but it is the one that ought to interest the insurance industry most, as one day it might be relevant for liability insurance. The focus is therefore on products and applications that come into contact with human beings, or that may affect the environment.

3 "Nanotechnology: Shaping the World Atom by Atom". www.nano.gov

Only recently has this problem come to the attention of legislators. There are a number of publicly funded studies aimed at analysing the potential risks to society resulting from the increasing dissemination of products manufactured using nanotechnology. Both the *Environmental Protection Agency* (EPA) and the *National Nanotechnology Initiative* (NNI) in the US and projects sponsored by the European Commission are already addressing such questions.

The research institutes of some prestigious universities are also tending to earmark a part of their resources both for application-oriented research and for risk assessments.

The "bottom-up" and "top-down" approaches

In nanotechnology, a basic distinction may be drawn between the top-down and the bottom-up approach.

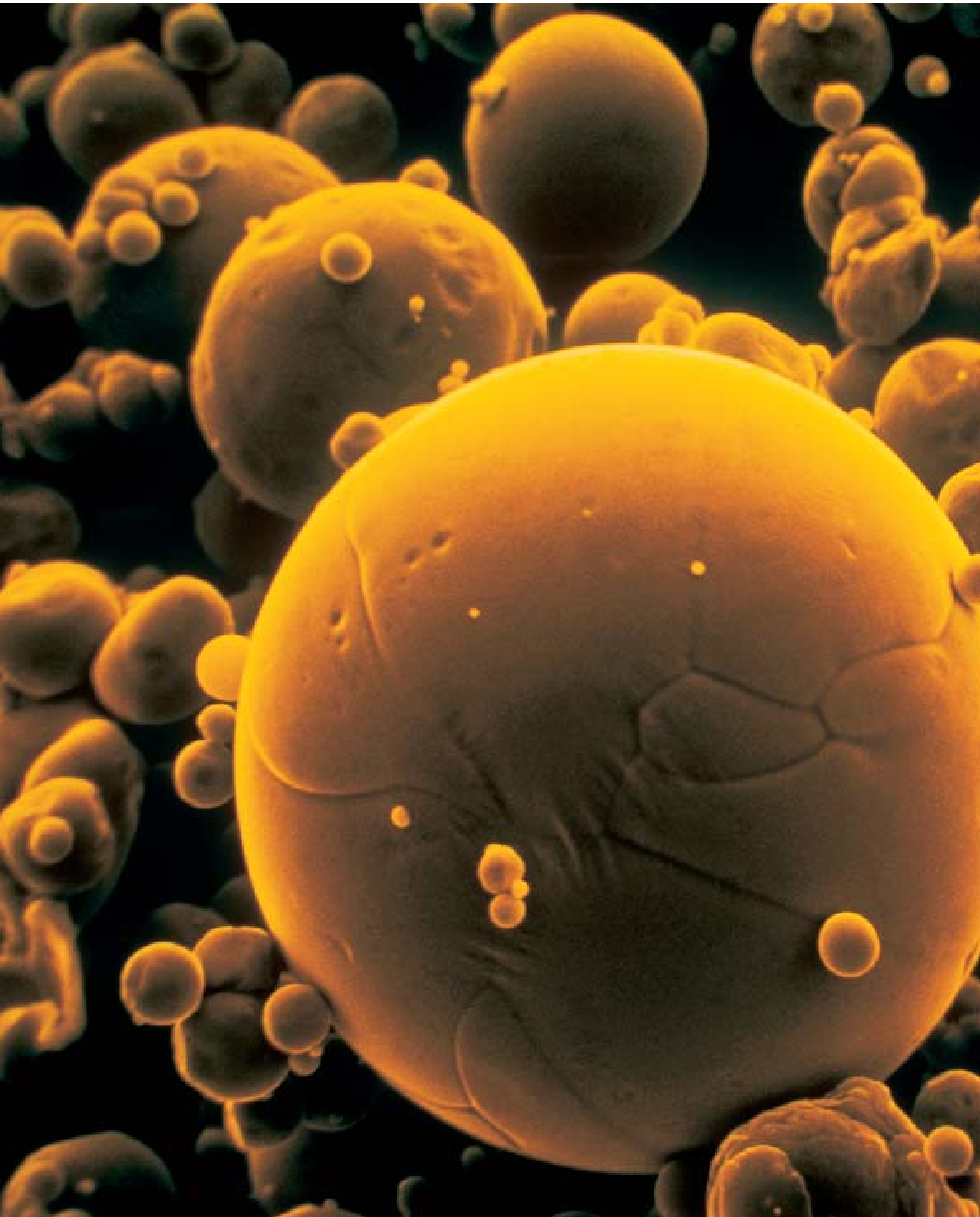
Top-down refers to processes in which a given bulk material is reduced in size to produce nanometre-scale particles, which are then either systematically inserted into larger structures or used as an admixture to other materials. This process is energy-intensive, waste-heavy and involves an extravagant use of resources. At the same time, the manufactured materials can be of great benefit, given their improved properties.

In the *bottom-up* approach, larger structures are built up atom by atom or molecule by molecule, or are allowed to grow through self-assembly. Many scientists hope that self-assembly and reproduction will yield completely new methods for the industrial manufacture of matter. Nature's biological methods of production may offer secrets that can be used in industry, as well.
A living cell is the most successful "nanofactory" known to man. A whole human being can be created from a few cells. The cell contains all the genetic information needed to duplicate itself. It can process raw materials in order to grow, using only a fraction of them to generate energy. It can reproduce, repair and move itself about. At the same time, it can recycle "waste products" using only a modicum of energy to do so. By an analogous process, experts dream of being able to have whole objects "grow" out of nanoparticles.

"Self assembly" (self-organisation) is a method of integration in which the components spontaneously assemble, typically by bouncing around in a solution or gas phase until a stable structure of minimum energy is reached. Self-assembly is crucial to the assembly of biomolecular nanotechnology, and is thus a promising method for assembling atomically precise devices. Components in self-assembled structures find their appropriate location based solely on their structural properties (or chemical properties in the case of atomic or molecular self-assembly). Self-assembly is by no means limited to molecules or the nanoscale and can be carried out on just about any scale, making it a powerful bottom-up method for nanotechnology.[4]

4 www.nanoword.net

Titanium dioxide nanoparticles with a smooth surface may be used as an anti-adhesive coating for windows or spectacle lenses, for example.



2 Nanotechnology – primarily an order of magnitude

The term "nanotechnology" mainly refers more to an order of magnitude than to a specific scientific discipline. The word is used quite generally to mean the visualisation, characterisation, production and manipulation of particles smaller than 100 nm. This includes the manufacture of so-called nanomaterials – nanomanipulation, in which individual nanoparticles are systematically manipulated with the aid of special microscopes – and molecular nanotechnology, which is mainly concerned with "self-assembly". The field of nanomaterials has, however, seen the greatest progress, and some of its products are already available commercially.

A nanomaterial is any material that either contains a certain proportion of nanoparticles or even consists exclusively of them. Specialists distinguish between *nanoparticles* in general and what are known as *nanotube*s or *buckyballs*. Nanoparticles are small particles that arise in the course of miniaturising any given material, such as gold, carbon or silicate. They account for the great majority of processed nanomaterials. Nanotubes and buckyballs, on the other hand, are specially manufactured particles which do not occur in nature and have a typical crystalline structure. They are used in the field of electronics among others and are still difficult and relatively expensive to manufacture.

Nanotechnology currently embraces a broad spectrum of applications and products. Various definitions are used, and there is little agreement on nomenclature. For the purposes of this publication, a definition has been chosen that refers exclusively to nanoparticles, coatings or materials that are smaller than 100 nm and possess specific properties connected with their size. Products and applications that are larger than 100 nm are thus deliberately excluded. Such materials are often grouped under the term nanotechnology in order to attract attention and acquire research funding. This gives rise, however, to slight overlaps with the already familiar microtechnology and materials science, which deals with larger particles almost void of specifically new properties.

Nanoparticle
A nanoparticle is a tiny particle that generally consists of either one element or a simple compound (ie a core with a shell around it). Examples include titanium dioxide particles in suntan lotions or ferrous oxide particles as a contrast medium in imaging techniques (X-rays, for example). Nanoparticles frequently have properties which vary from the bulk material they derive from. The admixture of nanoparticles can cause certain effects, such as material strength, conductivity, optical properties or scratch-resistance. In general, special changes in electrical, magnetic, mechanical or chemical behaviour can be obtained.

Nanotube
The term "nanotube" generally refers to a hollow cylindrical nanoparticle that is nanoscale (1–100 nm) in diameter, but may be much longer. Nanotubes may or may not consist solely of carbon, but those that do are the most thoroughly researched and widespread.

Buckyball
Buckyballs, also known as Buckminster Fullerenes, generally consist of exactly 60 carbon atoms, similar in structure to the pentagons and hexagons on a football. Since buckyballs are hollow, they can be filled with a substance, eg a contrast media. An outer coating is also possible, which obviously changes the properties of the buckyball. From a technical point of view, they function as semiconductors and are soluble in organic solvents.

2.1 Small particles with a large surface area

What makes a nanoparticle so unique? Particles in the nanometre range have two particular properties. First, anything smaller than about 50 nm is no longer subject to the laws of classical physics, but of quantum physics. This means that nanoparticles can assume other optical, magnetic or electrical capabilities that distinguish them clearly from their larger relatives in the particle family. Second, with decreasing size, the ratio between mass and surface area changes. This is because the smaller a body becomes, the greater its surface area becomes in relation to its mass.

"I wouldn't want to suggest that this stuff is dangerous. (...) We don't know that it's dangerous. The problem is, no one else knows."
***Pat Mooney, Executive Director of the ETC Group*[5]**

Their exceptionally large relative surface area enables nanoparticles to exert a stronger effect on their environment and to react with other substances. In particular, nanoparticles with a crystalline structure have more atoms on their surface that are less strongly bonded than those in the interior of the particle. Given their unstable situation, the atoms will try to change themselves: they are reactive. The smaller the particles, the greater the relative surface area. This also means, however, that there are proportionately more atoms on the surface and fewer in the interior.

In short, the smaller the particles, the more reactive the substance. This may well be desirable for catalytic purposes, but if such particles are inhaled, there could be harmful consequences. As size decreases and reactivity increases, harmful effects may be intensified, and normally harmless substances may assume hazardous characteristics. Expert opinions vary markedly over the potential risks associated with nanoparticles. While some scientists are confident that the benefits outweigh the risks, others believe that nanoparticles can harm living creatures through the very fact of their reduced size, regardless of what they consist of or how they were manufactured.

5 Martin Patriquin, "Small Matter Provokes a Major Debate," *Toronto Globe and Mail* (19 November 2003)

2.2 Natural and artificial nanoparticles

Are nanoparticles, then, fundamentally new? No, inasmuch as in nature and technical by-products, particles of nano-size have always been present. Salt nanocrystals are found in ocean air, for example, and diesel engines emit carbon nanoparticles. Cigarette smoke, burning candles and chimney fires also contain nanoparticles.

"Even with all its unknowns, even with all its perils and risks, who'd say no to nano?"
Ed Regis, science writer [6]

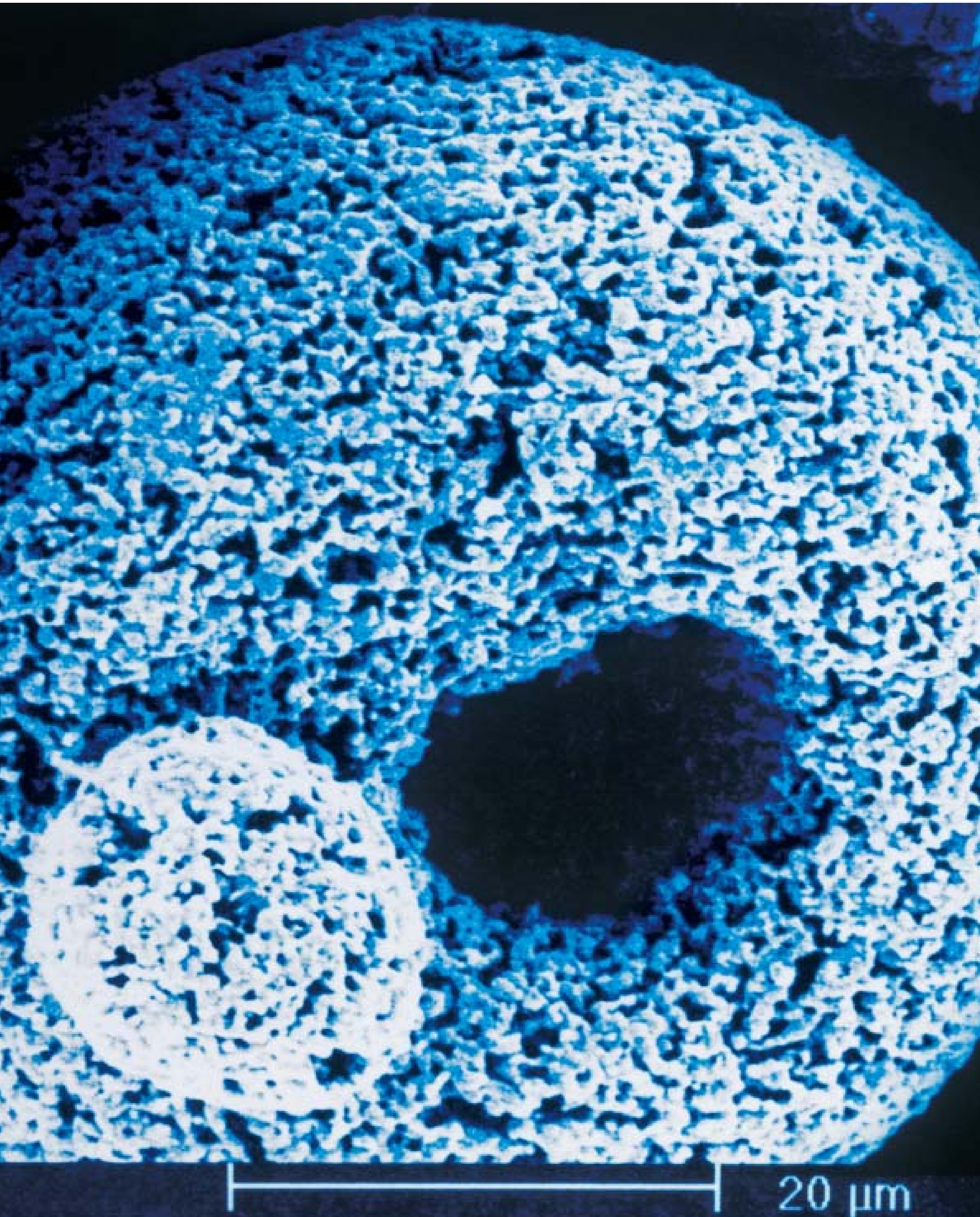
Nevertheless, only limited comparisons are possible between artificially manufactured nanoparticles and natural ones. Many of the nanoparticles occurring in nature, such as saline nanoparticles, are soluble in water. As soon as they are inhaled and come in contact with the tissue, they dissolve and lose their particle form. The nanoparticles from combustion processes – in motors, cigarettes or fireplaces – although not soluble in water, are very short-lived. They show a very strong tendency to agglomeration. In this way, they form larger particles and change from nanoparticles into microparticles, acquiring different properties.

On the other hand, artificially and commercially manufactured nanoparticles behave differently, so one cannot necessarily compare them with the "familiar" particles (eg from diesel exhaust fumes).

In general, nanoparticles have a tendency to agglomerate and get lumpy, which causes them to change into larger microparticles. These, in turn, are less reactive, less mobile and less well distributed – and as such, less interesting for the manufacturers and buyers of nanoparticles. The reason is simple. Larger particles may lose the desired properties and advantages typical of nanoparticles. Thus, in order to prevent an agglomeration of the nanoparticles, commercially available nanoparticles are often specially coated according to manufacturer specifications. Consequently, the particles in many commercial products – such as sprays or powders – remain reactive and highly mobile.

6 Ed Regis, *Nano. The Emerging Science of Nanotechnology: Remaking the World – Molecule by Molecule* (Boston: Little, Brown and Company, 1995)

Nanoparticles in porous spherical form photographed with the scanning electron microscope on a scale of 20 µm.



3 Through the human body: do all routes lead into the blood?

Human contact with nanoparticles takes various forms: they are inhaled with air, swallowed, and may possibly enter the body via the skin.

How do these particles behave on or in the organism? Underwriting risk analyses of products are all the more stringent, the closer the products come into contact with the body, since this means their potential to impair health is generally greater. A distinction is made as to whether a substance remains outside the body, remains on the surface of the skin or gains access to the body and gets into the bloodstream. Special attention is paid to particularly vulnerable organs such as the brain because foreign substances that are able to penetrate into such sensitive areas are considered to be particularly exposed to product liability. That is why, in assessing nanotechnology, we must have exhaustive knowledge of possible entry routes into the body.

3.1 Inhalation of nanoparticles

A number of products that are used in sprays – and hence can potentially be inhaled – contain nanoparticles. These include disinfectant or air-freshener sprays, dyes and paints, and sprays for impregnating clothing or porous materials, such as wood or clay. It is clear that nanoparticles are not only emitted by finished products, but also in the manufacturing phase. Especially in the case of spraying techniques that are used for coatings, large quantities of particles can be released as dust.

Deposits: deeper and more intensive
It is assumed that nanoparticles in the respiratory passages can cause a different kind of harm than that caused by larger particles. The type of harm is presumably based on modes of behaviour that apply to all nanoparticles without exception, regardless of their composition or form.

How deeply particles, can, in fact, penetrate into the lungs depends on their size. The lung is a relatively well protected organ. Inhaled particles first pass through the windpipe before reaching the lung tubules and bronchioles, which are lined with a dense mucous layer. It is here that the first particles to penetrate, above all the larger ones, are intercepted and borne away by the continuously upward heaving mucous layer; most of them are then exhaled.

Particles that penetrate more deeply get into the pulmonary alveoli, which are located at the ends of the ramified lung bronchioles and provide another protective shield: the so-called macrophages or "phagocytes". These specialised cells absorb foreign substances and eliminate them. Nanoparticles are absorbed by these phagocytes, and a considerable number can become deposited on the lung tissue without being exhaled again. As it is in the pulmonary alveoli that the oxygen exchange with the blood takes place, it would be possible for the nanoparticles to enter the bloodstream here.

The smaller the size, the greater the harm?
If equal quantities of nanoparticles – or larger particles of the same substance – are inhaled, the smaller particles cause a reaction in the lung tissue that is many times stronger.

Depending on the base material of the particle, changes of varying intensity have been detected. Astonishingly, even substances considered completely harmless in themselves – such as particles of latex – can have highly detrimental effects. Some scientific studies indicate, however, that the same principle applies in equal measure to all substances: the smaller, the more harmful.

The smaller, the more reactive
There are two mechanisms that could be responsible for this behaviour. One is the surface reactivity of the nanoparticles which, depending on the particle coating, can harm the surrounding tissue through chemical activity. The other is the overloading of the phagocytes that are responsible for eliminating the particles. If the number of invading particles exceeds a certain limit, the "eliminators" are overloaded. 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. In the event of a cold, the organism would be further weakened, because the process of deactivating potential pathogens would be slowed down. Overload symptoms occur even in the case of the most harmless substances, providing they are exogenous and not soluble in water. Larger particles can also overwhelm the phagocytes. There are, however, indications that the load on these cells depends on the total surface area of the particles or on the total number of particles. As nanoparticles have a much larger total surface area (and total number of particles), their effects could be more harmful.

Free radicals
The surface reactivity of the nanoparticles can, depending on the type of coating, cause chemical damage to the surrounding tissue. It is based on the formation of what are known as "free radicals", ie atoms that possess an "unsatisfactory" number of electrons. They are either over or under-endowed with electrons and thus in an excited state. As such, radicals are highly reactive, because they can snatch electrons from neighbouring atoms or force electrons onto them. In this way, free radicals optimise their own structure, but at the same time, transform another atom into a radical, thus triggering a chain reaction. If such radicals are also able to move freely, they can produce effects in the entire body and in all parts of the cell. Certain structures, such as the cell walls or the idioplasm, have been shown to be harmed by such free radicals.

In biological processes, free radicals are nothing unusual. They are commonly found in completely normal, healthy cells. At the same time, however, these processes take place under controlled conditions and locally. The harmful radicals whose effects are reinforced by environmental impacts are another story. Intensive sunbathing, for example, produces a similar effect: solar radiation causes cells in the body to become "stressed" and stimulated, which leads to the emission of free radicals that harm the tissue and – in the worst case – can contribute to the formation of tumours.

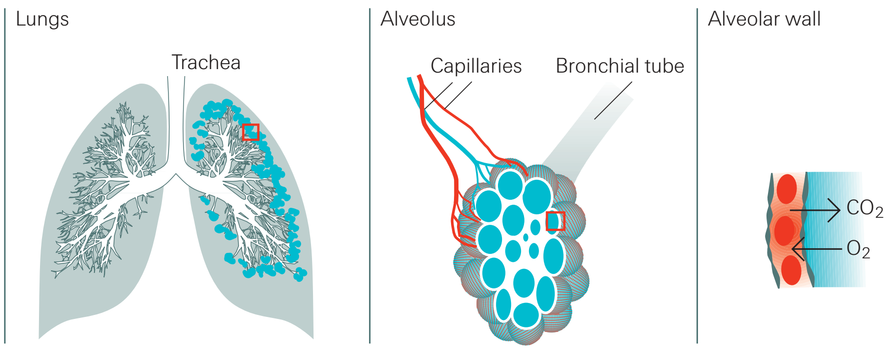
The harmful effects of free radicals nevertheless have a basically useful function in the body, since with their help, defence cells can destroy unwanted invaders, such as bacteria. The effect of free radicals is still subject to debate. How much significance is ultimately assigned to the harm caused by radicals presumably depends on how frequently and on what scale such reactions occur in the body. Science will likely face even a greater challenge over the key question of threshold values. Whether one can really speak of lasting damage to the tissue remains to be seen.

From the lungs into the bloodstream

Laboratory experiments have repeatedly shown that certain inhaled nanoparticles can also enter into the bloodstream. Although the relative quantities are quite small, it is still a new phenomenon for exogenous, insoluble particles to be absorbed from the lungs into the blood. Just how the particles get into the bloodstream has not yet been definitively explained. We do know, however, that some of the nanoparticles, when inhaled, are transported directly to the brain. The route leads through the nasal mucous membrane. If particles are deposited on the olfactory fibres in the nasal mucous membrane, they may proceed directly to the olfactory centre of the brain via the nerve cells in the nose. And, indeed, a case of such a transport has been recorded. Whether the particles continue to move about inside the brain and, if so, how they behave there, has yet to be determined.

Alveolus

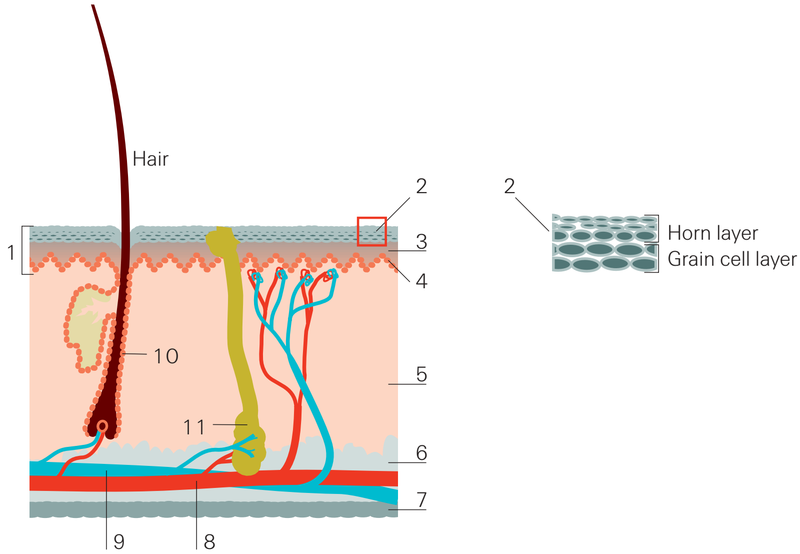
Alveoli are tiny thin-walled air sacs in the lungs that are supplied with oxygen-rich air from the bronchial tubes and are surrounded on the outside with fine blood vessels. This network of vessels can absorb oxygen from the alveolus and transport it throughout the whole body. The insides of the alveoli are lined with phagocytes (macrophages) that can absorb inhaled particles or bacteria and contribute to their elimination.



3.2 Particle absorption through the skin

Can nanoparticles permeate the skin and be absorbed in the blood? Specialists are still debating this, but it is imperative that a definitive answer be found soon, as many of the commercially available cosmetics, suntan lotions and baby products contain a considerable amount of nanoparticles. A number of products use nanoparticles as vehicles for osmophores, moisturisers or dyes of the kind used in cosmetic articles, shampoos, deodorants and in the softening agents of detergents.

Absorption through the skin
The top layer of skin consists of calloused cells without blood supply which do not constitute a solid barrier. Instead, the cells are layered and stacked, which causes interstices with an approximate width of 50 nm to form. The skin tissue beneath them is supplied with blood, as are the deeper layers of skin where the roots of hair are embedded. The fine hairs pass through a channel to the surface of the skin, thus linking the calloused surface with the deep layers of skin. Conceivable routes for the absorption of nanoparticles via the skin would therefore be either the passage through the calloused upper layer to the deeper layers of skin or the direct way via the roots of the hair to the bloodstream.



1 Epidermis
2 Disk epithelium cells
3 Prick cell layer
4 Basal cell layer
5 Dermis
6 Subcutaneous fatty tissue
7 Fibre connective tissue
8 Arteriole
9 Venula
10 Hair follicle
11 Sweat gland

Studies carried out to date have reached no agreement as to whether nanoparticles can, in fact, be absorbed via the skin. On the one hand, there are indications that previously marked nanoparticles can be detected in the blood. On the other, some scientists believe that the smallest particles cannot even penetrate to the bottom level of the top, calloused layer of skin. Why such disparate research results? The reason presumably lies in the different examination methods used. Some studies, for example, are not based on the skin of living organisms, but use detached pieces of skin unsupplied by blood which makes them only of limited relevance. Certain preparation techniques are also critical, because they may wash out the smallest particles before they can be detected.

Perhaps the only certainty is that no one knows at present how or how many particles can potentially be absorbed. Considering the wide variety of products already on the market, the need for a solution is urgent. The suntan lotions and skin creams used for babies and toddlers that contain nanotechnologically manufactured titanium dioxide are but one example. Titanium dioxide absorbs ultraviolet rays, thus offering protection against solar radiation. In the form of nanoparticles, its hypoallergenic properties – those incapable of causing allergies – make it particularly suited to sensitive skin. Although titanium dioxide was added to suntan lotions in the past, it was in the form of larger particles, and they tended to remain on the surface of the skin. In the new form, some of the titanium dioxide could possibly enter the body, however. Should there be proof that nanoparticles can penetrate the skin, particular care must be taken in using products containing them on small children, who have a particularly large skin surface in relation to their body weight.

Adding titanium dioxide to suntan lotions in the form of nanoparticles is considered a product enhancement. The advantage to the cosmetics customer is that particles of nano-size are transparent, and the suntan lotion no longer has to be applied to the skin in the form of a white mass. Furthermore, one assumes that a large number of small particles will offer better protection against the sun.

3.3 Particle absorption via the alimentary canal

Sooner or later, most substances that enter the body and are swallowed will arrive in the intestine. What happens to nanoparticles that we ingest with our food? Do they remain in the intestine or also pass into the blood system?

The intestine basically performs two tasks: it ingests food and protects the body from undesirable substances. The “desirable” substances are carried along specific transport routes to the intestinal cells, while foreign substances are usually retained in the intestine and then excreted. Drugs and vitamins are also absorbed via these transport mechanisms.

Nanoparticles, are absorbed via another route, that of the so-called "Peyer's plaques". These plaques are smallish nodules in the intestinal tissue that are actually part of the immune defence system. They are able to absorb larger molecules in "bubbles" and transport them right through the cell. If the content emerges at the other end, it gets into the lymphatic system from whence nanoparticles can pass into the blood system and spread through the body. As a general rule, the smaller the particles, the more of them are absorbed and the deeper they penetrate. Particles of under some 300 nm can reach the bloodstream, while particles that are smaller than 100 nm are also absorbed in various tissues and organs.

Possible sources for nanoparticles in the digestive tract include not only drinking water and food additives, but also dust from the atmosphere that settles on food, or traces of toothpaste that are inadvertently swallowed. More and more nanotechnologically manufactured fillings and implants are also being used in the field of dentistry, as they are supposed to have improved material properties. Abrasion or other processes, however, could mean that the processed materials enter the alimentary canal. If nanoparticles enter the digestive system via the routes described and proceed from there into the bloodstream, they can move throughout the entire body and behave in ways that may be detrimental for the organism.

"Fundamental changes in drug production and delivery are expected to affect about half of the USD 380 billion world-wide drug production in the next decade."
LaVan and Langer, Massachusetts Institute of Technology (MIT)[7]

3.4 Nanoparticles in the body

Nanoparticles can enter the bloodstream indirectly via the lungs or the digestive tract, or be injected into it directly in the form of drugs. Since nanotechnology gives rise to unexpected possibilities, recent developments in the pharmaceutical industry are very promising. Not only are the soluble and absorbent properties of drugs being improved, but "multifunctional active agents" are being newly created. It is now possible, for example, to include several active substances in the vehicle and to add an antibody that helps pinpoint the exact part of the body where the drug is to take effect. Or one can attach another particle to be used for imaging techniques. An appropriate coating of the nanoparticle lengthens its retention time in the bloodstream, so that the effect of the substance can be prolonged.

7 D. A. LaVan and R. Langer, "Implications of Nanotechnology in the Pharmaceutics and Medical Fields," M. C. Roco and W. S. Bainbridge, editors, *Societal Implications of Nanoscience and Nanotechnology* (2001): pp. 77–83.

"Nanotechnology-based goods and services will probably be introduced earlier in those markets where performance characteristics are especially important and price is a secondary consideration."
Roco and Bainbridge, US National Science Foundation (NSF)[8]

Experts assume that medicines and pharmaceuticals will be among the first nanotechnologically manufactured products to conquer the market. As a sector in which the quality and effectiveness of a product are of prime importance, the medical market offers enormous growth potential. Patients are prepared to accept higher prices as long as they believe in the remedy's effectiveness. The leaders in the development of pharmacological substances and innovative remedies in the nanotechnological sector are the US and, in second place, Europe. Hence, the North American pharmacological industry is expected to manufacture the first nanotechnological products. This will certainly be a challenge for the insurance industry, as potentially vulnerable products will find themselves confronted by an extremely sensitive legal system.

Country specialisations
The number of respondents identifying each country as the location for the most sophisticated nanotechnology developments in a particular industry.
(Based on a 3i survey of leading scientists, investors and management from the economic and industrial sectors.)

	Medical/ Pharma	Materials	Chemicals	Electronics	Manufacturing
Rank 1	US: West (28)	US: West (28)	Germany (25)	Japan (34)	US: West (26)
Rank 2	US: East (26)	US: East (27)	US: West (19)	US: West (33)	US: East (26)
Rank 3	UK (23)	Japan (25)	US: East (16)	US: East (20)	Japan (21)
Rank 4	Germany (19)	Germany (21)	UK (11)	Korea (17)	Germany (15)
Rank 5	Switzerland (9)	UK (15)	Japan (10)	Taiwan/ Germany (9)	Korea/ Taiwan (7)

Source: 3i: "Nanotechnology – Size Matters. Building a Successful Nanotechnology Company." White Paper, 10 July 2002.

While most pharmaceutical nano-products are still in the development phase, some are going through their final tests and are expected to be launched on the market soon. Undoubtedly, the potential for innovation is enormous. The new opportunities offered by nanotechnology could lead to therapies that would exterminate diseases currently held to be incurable. Particular hopes are placed on new diagnostic possibilities, innovative cancer therapies and the treatment of infections and brain diseases. New ways of administering drugs that improve their effect on the body and entail fewer side effects are also being researched and have already yielded successful results in individual studies. Various products used in *imaging techniques* are already available. Nanotechnologically enhanced products have also become established in the fields of tooth and bone implants as well as in disinfectant adhesive plasters and bandages.

Imaging techniques
The term "imaging techniques" was coined in connection with medical diagnosis. It is a collective term for techniques that make it possible to represent the structures of the human (and animal) anatomy in visual form [X-rays, computer tomography, angiograms, nuclear magnetic resonance (NMR) tomography, magnetic resonance imaging (MRI), etc]

Absorption in the body
What happens to nanoparticles that are either absorbed involuntarily from the environment or deliberately introduced into the body for medical purposes? Normally, exogenous particles or foreign substances that enter the bloodstream are absorbed – as we have seen – by specialised phagocytes that are responsible for removing such "foreign bodies". Oddly enough, however, this does not necessarily apply to nanoparticles. Everything smaller than about 200 nm is no longer specifically absorbed by these phagocytes, but – apparently without reason – by cells that are not actually "designed" for this function. Thus, nanoparticles can suddenly turn up in blood cells. This has also been demonstrated with a number of other cell types. Once absorbed by the cell, nanoparticles can thus travel through the blood and move at random throughout the entire body.

8 M. C. Roco and W. S. Bainbridge, editors. *Societal Implications of Nanoscience and Nanotechnology* (Arlington: National Science Foundation, 2001)

Distribution in the body and excretion
Nanoparticles can become widely disseminated via the bloodstream, thus penetrating to various organs such as the heart, bone marrow, ovaries or muscles. We have already established that nanoparticles have repeatedly been detected in the brain, the human being's best protected organ. Since nanoparticles are not restrained by any tissue barriers, it could be possible for them to gain access to a foetus via the placental barrier, as well.

Do the nanoparticles remain in the body for long periods of time? If not, can they still do damage? In time, the particles will most likely be excreted from most organs since, like every other foreign substance, nanoparticles are covered with a protein layer which marks them as a foreign substance. In this way, they are identified by the specialised phagocytes, which absorb and remove them from the body.

It is not always possible, however, to mark a particle in such a way as to identify it as a foreign substance. Depending on the type of particle coating, certain nanoparticles apparently fail to be identified and hence are not marked. They remain in circulation longer and are better able to spread through the body. After a few days or weeks, most of these particles can be found in the organs which contain particularly large numbers of phagocytes, namely in the liver, spleen, bone marrow and lymph nodes. The exact distribution of the nanoparticles among these organs depends on their individual coating and hence on their "surface chemistry". What happens to the nanoparticles subsequently depends on the material composition of the particle in question. Biodegradable substances are decomposed, their waste products then excreted via intestine and kidneys. Up to now, the pharmaceutical industry has focused on biodegradable materials almost exclusively as carriers for drugs.

"A friend of mine (Albert R. Hibbs) suggests a very interesting possibility for relatively small machines. He says that, although it is a very wild idea, it would be interesting in surgery if you could swallow the surgeon. You put the mechanical surgeon inside the blood vessel and it goes into the heart and ‹looks› around. (Of course the information has to be fed out.) It finds out which valve is the faulty one and takes a little knife and slices it out. Other small machines might be permanently incorporated in the body to assist some inadequately-functioning organ."
Richard P. Feynman, Nobel Laureate, Physics, 1965 [9]

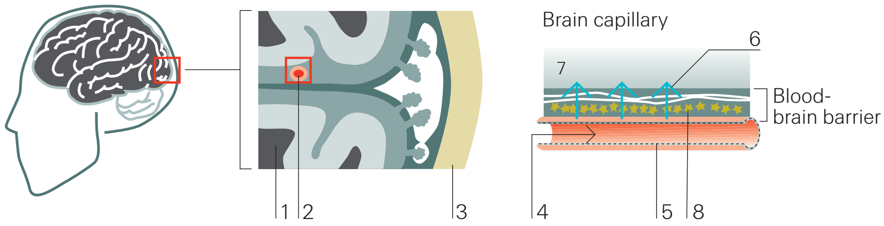
Although the behaviour of non-biodegradable nanoparticles has been studied far less, it seems possible that they are deposited in certain organs, especially in the liver, where they accumulate. The duration of deposits there, the potential harm they may trigger, and what dose might cause a harmful effect have not yet been exhaustively examined. Other diseases of the liver indicate, however, that even the accumulation of completely harmless substances can impair and damage the functioning of that organ.

Nanoparticles in the brain
The brain is the best-protected organ in the human body – for good reason. The organ's extremely sensitive nerve cells are dependent on a precisely defined milieu to retain their ability to function. An extremely strict entry control as much as prevents any foreign substances from passing into the brain. Even the blood vessels that supply the whole body have no direct access to the brain tissue: they only touch the outside. The term used for this is the *blood-brain barrier*.

Whereas in most types of tissue, the transported substances can leave the blood vessels, the vessels in the brain are well sealed. The only way of entering is by what is known as active absorption. The blood vessels are lined with special cells that recognise nutrients and other substances, actively absorb them and pass them on to the brain tissue.

9 Richard P. Feynman, *There's Plenty of Room at the Bottom. An Invitation to Enter a New Field of Physics* (1959)

Blood-brain barrier
For the brain cells to function, the milieu in the brain must remain constant. In order to ensure that not just any substances can get into the brain, the vessels supplying the brain are lined with a thick layer of endothelial cells. On the outside this network of vessels is surrounded by a further layer of astrocytes that only permit a controlled passage of substances from the blood into the brain.



1 Brain
2 Artery
3 Cranial bone

4 Blood flow
5 Endothelium
6 Water, oxygen, glucose
7 Liquor
8 Astrocytes

This transport route is extremely selective; more than 98% of the drugs that are supposed to have an effect on the brain fail to clear the blood-brain barrier. In order to produce even the slightest effect, the drug dose may have to be so high that considerable side effects can occur. There are few exceptions to this; a few liposoluble substances, such as alcohol or caffeine, for example, are able to pass through readily. To bring substances through the barrier that are strongly rejected by the brain, the active substance is attached – in the drug's development – to a carrier which has natural access to the brain and "smuggles" it across.

It is not surprising, therefore, that the pharmaceutical industry places great hopes in nanotechnology. A nanoparticle used as such a carrier with a drug attached has shown in experiments to have a markedly increased concentration in the brain. Nanoparticles can evidently gain access to the brain, while individual drugs cannot. Research has shown that, depending on the coating of the nanoparticle, the degree of drug absorption can be increased even further. As regards passage into the brain, whether the nanoparticles make the barrier permeable and slip between the cells, or "dupe" the cells into absorbing them is still subject to discussion.

Without question, nanotechnology promises to open completely new horizons for the manufacture and application of drugs. It might also herald reductions in drug doses for the treatment of illnesses, thus imposing less strain upon the body. It might make possible the introduction of substances to the brain that the organ would normally resist altogether, thus enabling treatment of illnesses hitherto considered incurable – bringing hope for terminally ill patients, on the one hand, and possibilities of economic growth for the pharmaceutical industry, on the other.

Unfortunately, however, we must assume that such products will also entail new risks, risks that have not yet been recognised as such. What happens if certain particles enter the brain that were not intended to reach it? What if nanoparticles injected into the blood stream to treat a tumour, say, were also to find their way into the brain? Depending on its texture, the particle could circulate in the blood for a shorter or longer period of time, only to be finally deposited in the brain. As no one knows precisely when and how many of these particles are broken down again and excreted, it is conceivable that they may accumulate, which would mean a lasting change in the brain's highly protected milieu. Neuro-degenerative diseases, such as Alzheimer's or Parkinson's, are thought to be caused by a disruption of the iron concentration there. Yet, iron oxide nanoparticles are already being used for a number of applications – as a new kind of contrast medium in magnetic resonance scans, for example. Unfortunately, many side effects are only discovered after a lapse of time; several years may pass before fully unexpected risks are revealed, and they may only be understood in retrospect.

3.5 Interaction with biological processes

The body is subject to countless regulatory and control processes, each finely attuned to one another. Active proteins known as *enzymes* help keep our body temperature constant, regulate sensations of hunger and sleep, provide the body with all vital substances and help resist infection. An impairment of these processes can trigger a whole flood of reactions that interrupt normal bodily functions and, in the worst case, do them irreversible damage.

Enzymes
Biocatalysts; macromolecules, generally proteins, that catalyse chemical reactions in biological systems. An enzyme is a biochemical catalyst that helps to split or otherwise modify a substrate. The enzyme facilitates the necessary reaction by reducing the activating energy, which always has to be overcome for metabolism to take place at all. The enzyme takes part in the biochemical reaction and even forms a temporary compound (the enzyme-substrate complex) with the substances to be converted, but is not modified by the reaction.

Enzymes are by their chemical nature proteins. Responsibility for the catalytic effectiveness rests with the so-called active centre that consists of specially folded parts of the polypeptide chain or reactive non-protein elements of the enzyme molecule. A special hollow structure in the enzyme enables the active centre to make contact with a suitable substrate.[10]

Given that nanoparticles can readily gain access to the body, one questions whether they can also affect its regulatory mechanisms. The messenger substances and enzymes controlling these processes measure some 20 nm across and function according to the key-lock principle. Only substances that fit exactly into the place provided for a given purpose and can dock there will activate the enzyme, which then performs a certain task. Enzymes normally come and go and do not block any natural processes irreversibly.

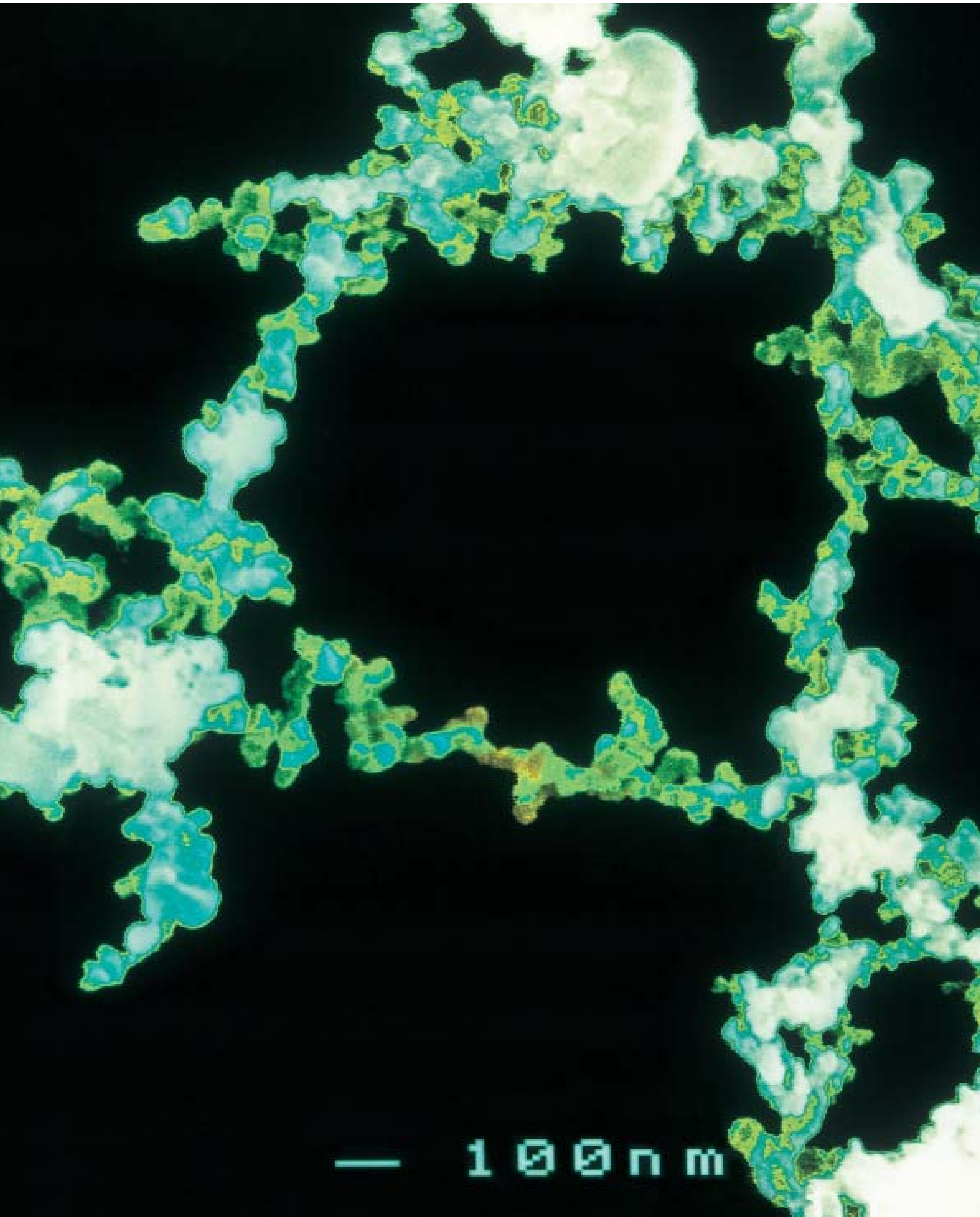
In some cases, nanoparticles have disrupted biological processes, causing impairments, for example, to structural or metabolic processes. Where exchanges take place between enzymes that can be intercepted or interrupted by nanoparticles, communication between neighbouring cells also seems to be influenced. Under certain circumstances, nanoparticles might also cause problems for the immune system. Either, because – individually – they are so small as not to be recognised at all and only attract the attention of the immune system when they are deposited on biological structures (and trigger undesirable reactions), or because they are detected and trigger systemic disorders such as allergies.

10 www.net-lexikon.de

Research in these fields, too, is still in its infancy. Whether – and to what extent – the new technology can affect the body is still a matter of speculation. The body's many repair and compensatory mechanisms must be taken into account. Clearly, however, a great deal more information is needed to determine the possibilities of interaction between nanoparticles and the body.

Having looked at the potential risks, one should also consider the inherent opportunities. The disruption of certain biological processes can also be deliberate with a view to achieving a desired effect. A well-researched example of such a disruption is the partial inhibition of the AIDS pathogen with the aid of a "buckyball". Such "buckyballs" can block an enzyme necessary for the multiplication of the virus by assuming and holding a position in the enzyme's docking site. The intention is to achieve a lasting and irreversible inhibition of the enzyme.

Diesel carbon nanoparticles magnified 45,000 times by
the scanning electron microscope.



4 Nanoparticles in the environment

Depending on the techniques used in manufacturing them and given their widespread dissemination, nanoparticles can be released into the water or the air and ultimately contaminate the soil and the groundwater. Furthermore, nanoparticles are increasingly being used in all kinds of disposable articles that, sooner or later, have to be recycled or removed as waste. Further, many of the artificially manufactured nanoparticles will be new to the environment in type and quantity. They could constitute a completely new class of non-biodegradable pollutants, with which scientists, obviously, are still unfamiliar. The long-term behaviour of such substances and their effects on the elements are thus extremely hard to foresee.

On the other hand, efforts are being made towards using nanotechnology to protect the environment. State-funded research projects, especially in North America, are already assessing whether nanoparticles can be used to clean up contaminated sites after cases of widespread environmental pollution. Skirting the expense of pumping up and treating 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. Using today's techniques for dealing with large-scale industrial contamination, the soil has to be removed cubic metre by cubic metre, treated and brought back again – a costly and lengthy procedure.

"(Nanotechnology) holds the answer, to the extent there are answers, to most of our pressing material needs in energy, health, communication, transportation, food, water, et cetera."
Richard Smalley, Professor, Rice University and Nobel Laureate, Chemistry, 1996[11]

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, ground water or air and "neutralise" them. Further, nanoparticles that contain silver and have an antibacterial effect are currently being tested for processing drinking water.

Magnetic techniques and special filtering methods may be used to reclaim the particles used. Having done their job, the particles would ideally remain at the site where they were used, as they are either biodegradable or able to form conglomerations. They can, therefore, be compared to larger materials that appear naturally in the environment.

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. Whereas select studies show promising results in environmental decontamination, there are few empirical values for the successful application of nanoparticles in industrial processes. Thus, any forecast of the long-term effects of such techniques remains uncertain. Other research projects focus on nanotechnological possibilities to save energy. The electronics sector could make significant savings by employing more energy-efficient devices.

11 ETC Group, *The Big Down* (Winnipeg, 2003): p. 46.

"This field is still in its infancy. The first papers and first results will have to be cautious. The field is growing so rapidly in the discovery end that questions about their environmental consequences are still being generated."
Joseph B. Hughes, Professor, Georgia Institute of Technology[12]

Parties with new solutions for dealing with increasing environmental pollution and depletion of essential resources, such as water of fossil fuels, will be sure to have their say. Particularly in view of the rapidly growing world population, solutions will have to be found. And the key question is this: how can we harness nanotechnology to ensure that it works for us?

As early as the year 2000, scientists in the US and UK supposed that nanoparticles could have undesirable effects on the environment. Studies on environmental questions, however, are still in the elementary stages – concrete results are not currently available.

Although little definitive knowledge is available on how nanotechnologically manufactured products behave in the environment, such products are already in use today and more will be launched on the market in the near future. So, the approach to the opportunities and risks involved must be worked out now, the sooner and more comprehensively, the better.

Ultrafine particles (UFP)
Ultrafine particles are smaller than 100 nm. The term "ultrafine particle" is identical with that of "nanoparticle" and is used in this publication to refer to the particles in the air which have been familiar to scientists for some time.

In the absence of conclusive evidence, scenarios have to be devised and possible findings borrowed from related fields. Based on what we know about worldwide air pollution, for example, we can make limited deductions about the behaviour of *ultrafine particles* in the air and their effects on health. Common features or differences between the new synthesised nanoparticles ultimately facilitate our understanding of their possible behavioural mechanisms.

Nanoparticles in the air
Decades of research have been devoted to pollution of the atmosphere and its influence on human health. In that connection, scientists have repeatedly studied the potential hazards to health represented by ultrafine particles (UFP).

Diesel engines, for example, emit ultrafine particles of amorphous carbon, thus contributing to air pollution, especially in urban areas. Some studies have demonstrated that the number of ultrafine particles in the air correlates to the mortality rate in the population. This applies particularly to the more susceptible children or elderly people. The particles studied, however, are dust from diesel exhaust fumes, which normally form clusters (aggregate) and settle spontaneously as deposits within a few days. Whereas this kind of dust is eliminated from the air after a certain period of time, artificial nanoparticles are often specially treated so as not to form clusters and thus remain airborne much longer. Such treated particles rarely land on surfaces and may lead to the reactions in the lungs mentioned earlier in this publication.

12 Barnaby J. Feder, "As Uses Grow, Tiny Materials' Safety is Hard to Pin Down." *New York Times* (3 November 2003)

Colloids
Particles that remain mobile in liquids because they do not form conglomerations and are not deposited. The particles may be either natural or artificial in nature.

Pollutants in the soil
Because they bond with water-repelling pollutants and heavy metals, *colloids* play a key role in the wide distribution of pollutants into the soil. The colloid substances studied to date are many times larger than the nanoparticles under discussion here. Owing to their larger surface area, the smaller nanoparticles may bond with more pollutants and transport them through the soil. If they were more mobile as well, pollutants would 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 "piggy-back" 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.

The chief precondition for the mobility of particles in the soil is saturation with water. Depending on the condition and chemical composition of the liquids and the water flow, particles are transported over longer or shorter distances. Whether and to what extent nanoparticles influence the behaviour of water is not yet clear, but even small changes are enough to influence ecological laws, changing not only the distribution of pollutants in the soil, but also the quality of the groundwater. Although there is now an awareness of this problem, the relevant research activities are still in their infancy.

Transport via the water cycle
Water evaporates under the influence of heat and is precipitated elsewhere in the form of rain. Via the water cycle, nanoparticles could spread rapidly all over the globe, possibly also promoting the transport of pollutants. Will we be able, in the future, to detect metallic nanoparticles in the polar icecaps? We may, but more importantly, we are taking the liberty of exercising our imagination. To do so helps us develop scenarios pointing to potential risks.

"It is difficult to convince scientists or funding managers to support environmental impact studies. The immediate payback for research that demonstrates ways of using nanomaterials to cure disease, for example, is greater than the reward for uncovering that nanomaterial may cause disease."
Vicki L. Colvin, Executive Director, Center for Biological and Environmental Nanotechnology (CBEN), Rice University [13]

Yet another effect on the climate is conceivable, if not very probable. The known nanoparticular mechanisms could either lead to atmospheric warming or cooling. The effect of nanoparticles on the climate has been difficult to determine to date. Yet, for the next few decades, it is unlikely that nanoparticles will become as major an issue as greenhouse gases.

Absorption of nanoparticles by plants
If the roots of plants were to absorb nanoparticles, the nanoparticles could enter the human and animal food chain through the consumption of crops. Conceivably, these nanoparticles could take some pollutants with them. Whether plants can also absorb nanoparticles from the air is still open to debate. Given that nanoparticles function as drug carriers in the human body and, in some cases, can penetrate its best protected areas, we can at most speculate about the absorption capacity of plants.

13 Vicki L. Colvin, "Responsible Nanotechnology: Looking Beyond the Good News," *EurekAlert! Nanotechnology in Context* (November 2002) www.eurekalert.org

Worst-case scenarios
In view of the prevailing uncertainties, worst-case scenarios easily come to the fore. What would happen if certain nanoparticles did exert a harmful influence on the environment? Would it be possible to withdraw them from circulation? Would there be any way of removing nanoparticles from the water, earth or air?

Clearly, the elimination of nanoparticles from the environment would be extremely difficult – a major challenge to the manufacturing industry. For nanomaterials' manufacture involves the hazard that manufacturing waste, like any other waste, will be released into the environment via emissions or effluents. Were this procedure to have far-reaching effects on the drinking water supply or the composition of the air, both industry and society would be faced with a daunting problem.

The removal of nanoparticles from liquids such as drinking water is currently only conceivable by means of *centrifugation* or *ultrafiltration*. Neither method is suitable for processing large volumes, as both are cost-intensive.

Centrifugation
Particles are separated from one another by means of centrifugal force caused by rapid rotation.

Ultrafiltration
Special method for filtering liquids through a particularly fine-meshed filter while applying pressure (0.7 – 4.8 bar).

In order to filter nanoparticles from the air, new filtering techniques are required, because the air-purification filters currently in use in buildings and manufacturing plants generally have pores too large to "catch" nanoparticles. It is not, however, possible to reduce the filters' pores to a size that would enable them to do so. Problems such as strong differences in pressure and pore blockage will have to be overcome first. These challenges show that effective face masks are not a very realistic prospect at present, since the requisite fibre design would render normal breathing impossible.

Yet as regards breathing masks, another approach is being adopted by a number of start-up companies. They are manufacturing particularly efficient protective filters with the aid of "nano-filters". As with the decontamination of polluted earth or water, highly reactive nanoparticles are attached to the fibres in the respiratory filter. The particles to be filtered out collide with the coated fibres and are neutralised and rendered harmless through a chemical reaction. While the success of these developments remains to be seen, experiments with the neutralisation of bacteria and certain chemical substances have apparently already yielded positive results.

Disposal or recycling?
How nanomaterials will react to current disposal and recycling techniques is an open question. Again, the paucity of answers is reason enough to start a dialogue.

New forms of energy for environmental protection

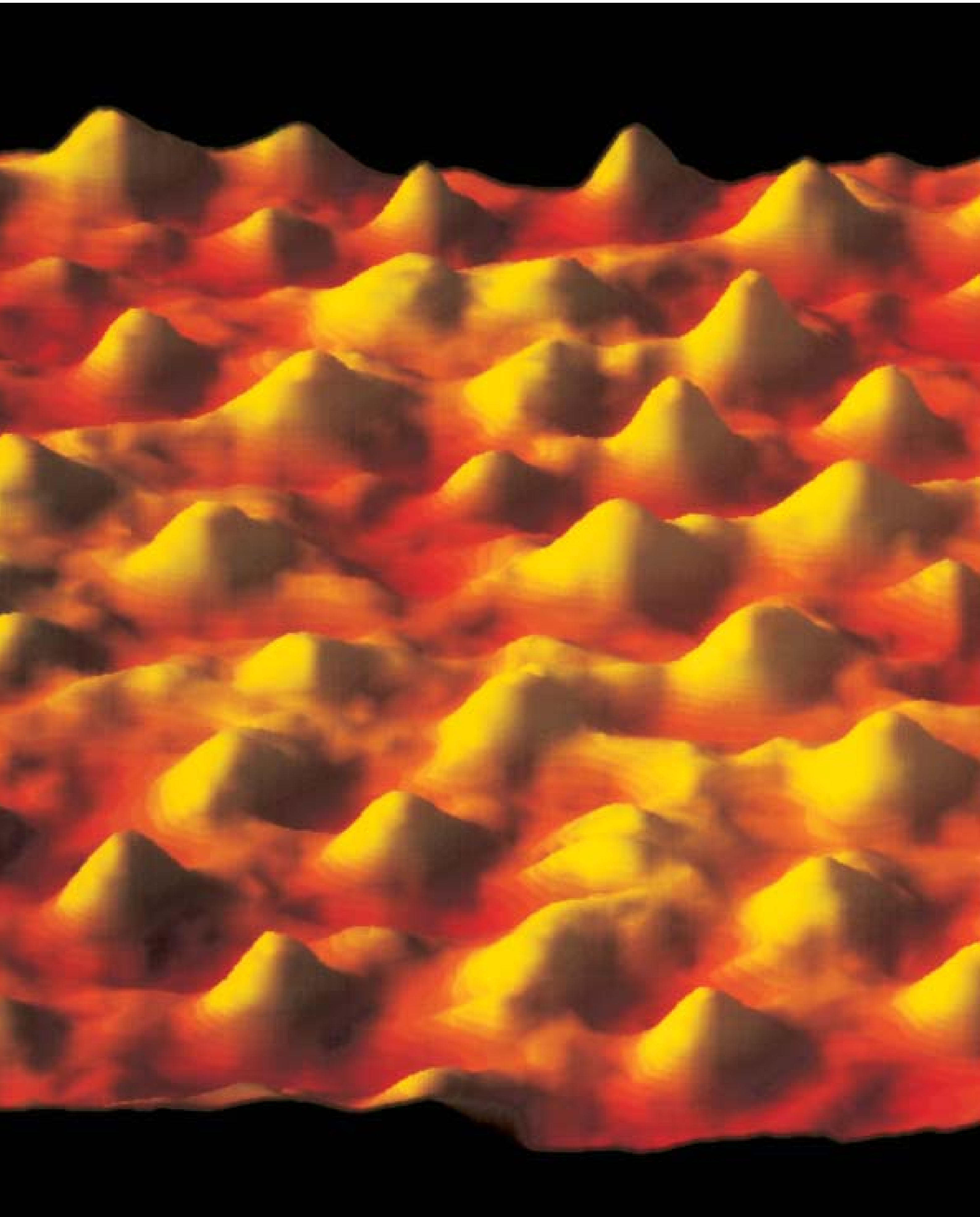
The enormous energy-saving potential of nanotechnology may also benefit the environment. New fuel cells in the form of nanotubes act as excellent hydrogen reservoirs, and innovative forms of lighting or new kinds of solar cells may, researchers assure us, be sprayed onto buildings or fit into clothing in the future.

Organic solar cells absorb sunlight with the aid of an applied coating of dye a few nanometres thick, which – analogous to photosynthesis in plants – transforms light into energy. Innovative lamps, known as organic light emitting diodes (OLED), also consist of an applied substratum of a thickness measured in nanometres that lights up when electrified. These lamps not only exceed the efficiency of conventional light bulbs, but are also cheaper to manufacture.

Although such applications are not yet marketable, their potential is obvious. Organic light and solar power generators are energy-saving and reasonably priced thanks to their organic source material, and mechanically flexible because of the thinness of the layer. Thus, organic light diodes could be used to create bend-and-fold computer displays or three-dimensional illuminations. There are no limits to the possible applications: examples include illuminated street signs, new lighting systems for cars and house interiors in which entire structural elements, such as ceilings, are used to emit light.

The opportunities created by nanotechnology consist, on the one hand, of new ways of saving energy, developing innovative sources of energy and making better use of existing resources. On the other hand, they offer new manufacturing techniques which require fewer raw and base materials and produce less toxic waste. Through reduced weight and the use of alternative fuels in transport and manufacturing, emissions of greenhouse gases could be reduced.

Carbon molecules stimulated to emit light by means of a scanning tunneling microscope (STM). The resolution is 5 nm.



5 Occupational hazards

"This ‹latency lacuna›, which is common to all long-latent-period hazards, is an illustration of the common error of assuming that ‹absence of evidence of harm› means ‹evidence of absence of harm›. It does not."
***David Gee and Morris Greenberg, science writers*[14]**

Most "nano-products" do not consist entirely of nanoparticles, but only contain an admixture of them. Nanoparticles that serve as raw materials are manufactured and packaged in specialised factories, where exposure at the workplace mainly takes place. During transportation, and especially during loading and unloading of semi-finished or end-products at the production facility, workers can also come into contact with the nanotechnologically manufactured materials and their inherent risks.

What effects can nanoparticles have on the health of those who handle them in their jobs? A distinction must be drawn between particles contained in powders and particles contained in liquids. The latter are easier to restrain and do not spread as easily. Powders, on the other hand, are disseminated by the slightest disturbance in the air. Nanoparticle powders that have been specially treated to prevent them from forming clusters have an even higher dissemination potential and remain longer in the air. Highly reactive particles, we have established, are especially critical for the workers exposed to them.

Many of the stages in the manufacture of nanoparticles take place in an closed environment, some of them in low-pressure chambers. But during the transport of the nanoparticles from the production facility to the application site, a certain degree of handling cannot be avoided, and as such, their distribution could constitute a hazard in the working environment. 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.

"In a field with more than 12,000 citations a year, we were stunned to discover no prior research in developing nanomaterials risk assessment models and no toxicology studies devoted to synthetic nanomaterials."
***Vicki L. Colvin*[15]**

To date, the risk of work-related exposure to nanoparticular substances has been measured in terms of the risk familiar from related, larger forms of particle. Titanium dioxide, a product manufactured in relatively large quantities, serves as a typical example. According to law, those who have to handle certain materials must be issued with Material Safety Data Sheets (MSDS), which describe potential risks and lay down suitable protective measures for handling. The safety data sheets for titanium dioxide nanopowder contain the industrial safety and health recommendations for "titanium dioxide", recommendations evidently adopted from those which were drawn up for the larger particle forms. Thus, the safety data sheet for nano-titanium dioxide powder still recommends that a dust respirator be worn while handling this substance, although such masks are known to offer only limited protection.

14 David Gee and Morris Greenberg, "Asbestos: from 'Magic' to Malevolent Mineral." *Late Lessons from Early Warnings: The Precautionary Principle 1896–2000.* EEA Environmental Issue Report, no. 22 (2001): pp. 52–63.

15 Vicki L. Colvin, "Responsible Nanotechnology: Looking Beyond the Good News," *EurekAlert! Nanotechnology in Context* (November 2002) www.eurekalert.org

Furthermore, the exposure limits were set for much larger particles and are, in fact, too high for nanoparticles. Regulations governing the transport of such powders are not specifically mentioned and, in the case of titanium dioxide, no distinction is made between the more reactive crystal form "rutile" and the less reactive form "anatase". Thus, a worker who handles catalytic titanium dioxide nanopowder wears a relatively useless face mask and works in a building with a ventilation system that is insufficiently equipped to remove the particles from the air!

Presumably, nanoparticles must be handled with the same care given certain bio-organisms or radioactive substances. Adequate protective measures, such as a nano-compatible "glove box", will probably have to be developed to ward off possible dangers.

Great innovation potential

Nanotechnology will change the world as we know it – it is probably only a question of time. Certain innovations have already established themselves, such as special surface treatments with water-repellent and self-cleaning effects on glass, plastic, metal and porous materials. Solar cells mounted on a roof will continue to look good as new even after prolonged exposure to the effects of heat, dust and cold. Nanotechnology plays a part in that.

The phenomenon of self-cleaning surfaces is based on a concept drawn from nature. The *lotus effect* was adopted from the Asian lotus plant, which hardly gets wet even after heavy showers; its leaves always remain immaculately clean. This is due to the special surface texture of the leaves:, composed, on the one hand, of extremely water-repellent wax crystals and, on the other, featuring a rough surface area in the nanometre range.

Raindrops come into contact with the leaf over only an extremely small area and roll off so quickly that they take any dust or foreign particles with them. Modelled on this principle, nanotechnology not only makes it possible to manufacture self-cleaning window panes and traffic signs, but also to impregnate porous materials, such as wood or clay, and thus protect the façades of buildings from the unwelcome attentions of graffiti artists.

More recent achievements made possible by particle technology include the scratch-proof paints favoured by car manufacturers and new forms of protection against corrosion which translate into the much thinner and lighter coatings of great interest to aircraft manufacturers and other industries. New anti-corrosive solutions for metals may soon replace the chromium compounds used in rust-proofing which are both extremely toxic and hard to dispose of. Surfaces manufactured using nanotechnology would thus make a viable contribution to environmental protection.

Figure 1

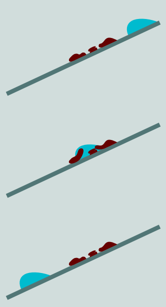
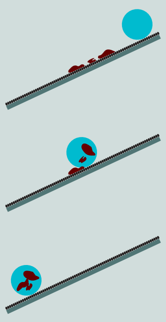


Figure 2



Lotus effect

Figure 1: Surface with high surface tension. Waterdrops spread to cover a large surface. Dust particles are not removed.

Figure 2: Surface layered with a nanostructure, which reduces the surface tension such that waterdrops roll off – a self-cleaning surface comparable to the lotus plant's.

Silicon dioxide (SiO_2) nanopowder mixed with nanodisperse fluid (colloidal solution) is used in water purification, for example, to filter out particles in the nano range. Photograph taken with the transmission microscope on a scale of 50 nm.

6 Regulatory context

Up until early 2004, nanotechnologically manufactured products were not subject to any special legislation. There were neither special regulations, recommendations on how such products or their base materials were to be handled, nor any obligation to label such products for what they were.

In view of the variety of products affected, this is not surprising. While the product range extends from drugs through textile fibres to glass and aircraft parts, nanoparticles themselves neither recognised as a separate class within certain product segments nor addressed accordingly. The Food and Drug Administration (FDA) classifies nanoparticles in ultraviolet screening substances – not as a new substance in its own right, but as a "variation of the bulk material", hence, a variation of the base substance.

Consequently, titanium dioxide nanopowder is treated in just the same way as the commonly available larger particles of the same substance. Since it is not a new substance, it need not be registered separately. Costly and prolonged testing procedures are thus rendered superfluous. The European Commission's Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers takes a similar view: titanium dioxide is classified as "safe", regardless of the size of the disseminated particles. The fact that the very miniaturisation of materials harmless in themselves may entail risks to health is not taken sufficiently into account.

"It is possible to speculate that inorganic matter is generally biologically inert. However, without hard data that specifically address the issue of synthetic nanomaterials, it is impossible to know what physiological effects may occur and, more critically, what exposure levels to recommend."
***Vicki L. Colvin*[16]**

This is remarkable, given that nanoparticles are distinguished from microparticles by several properties. Were this not the case, there would be no sense in replacing the larger microparticles in a number of products by more expensive nanoparticles.

The difficulties with the classification and registration of nanomaterials can be detected in the formulation used by the FDA: "substantially equivalent to conventional products". Yet there are sound reasons for placing nanoparticles in a class of their own. Nanoparticles can enter the body by other routes than those used by microparticles. They can penetrate parts of the body that are protected against larger particles and enter into the systemic circulation. They are also presumed to be more reactive, so that under certain circumstances, interactions harmful to health may ensue.

Nor, surprisingly enough, are the regulations concerning exposure to nanoparticles at the workplace very stringent. "Hazard guidelines" for airborne particles in the air have so far generally been based on two different systems:

The first limits the permissible quantity of known toxic substances in the air. This applies, for example, to asbestos, silicates, barium, chromium and many other substances for which the World Health Organisation (WHO) has defined internationally valid standards. Here again, the assessment of potential health hazards is based on the properties or the toxicity of the bulk material.

16 Vicki L. Colvin, "Responsible Nanotechnology: Looking Beyond the Good News," *EurekAlert! Nanotechnology in Context* (November 2002) www.eurekalert.org

"Never before have the risks and opportunities of a new technology been as closely linked as they are in nanotechnology. It is precisely those characteristics which make nanoparticles so valuable that give rise to concern regarding hazards to human beings and the environment alike."
Marcel Bürge, Risk Engineering Services, Swiss Re

The other regulates the level of airborne dust in general, including non-toxic forms of dust ("Total dust, containing no asbestos and less than 1% crystalline silica").[17] Germany, incidentally, is one of the first countries to advocate the introduction of separate regulations governing ultrafine particles – ie nanoparticles – in the air.

Nanoparticles and other substances manufactured using nanotechnology, such as buckyballs or nanotubes, have not yet been assigned to a separate class of substances. Nor is it clear whether this would be a good idea, because, depending on their individual size, coating, bulk material or composition, two "similar" nanoparticles can exhibit completely different properties. An iron particle with a coating not only behaves differently from one without a coating – what it was coated *with* becomes a criterion.

Challenge for research

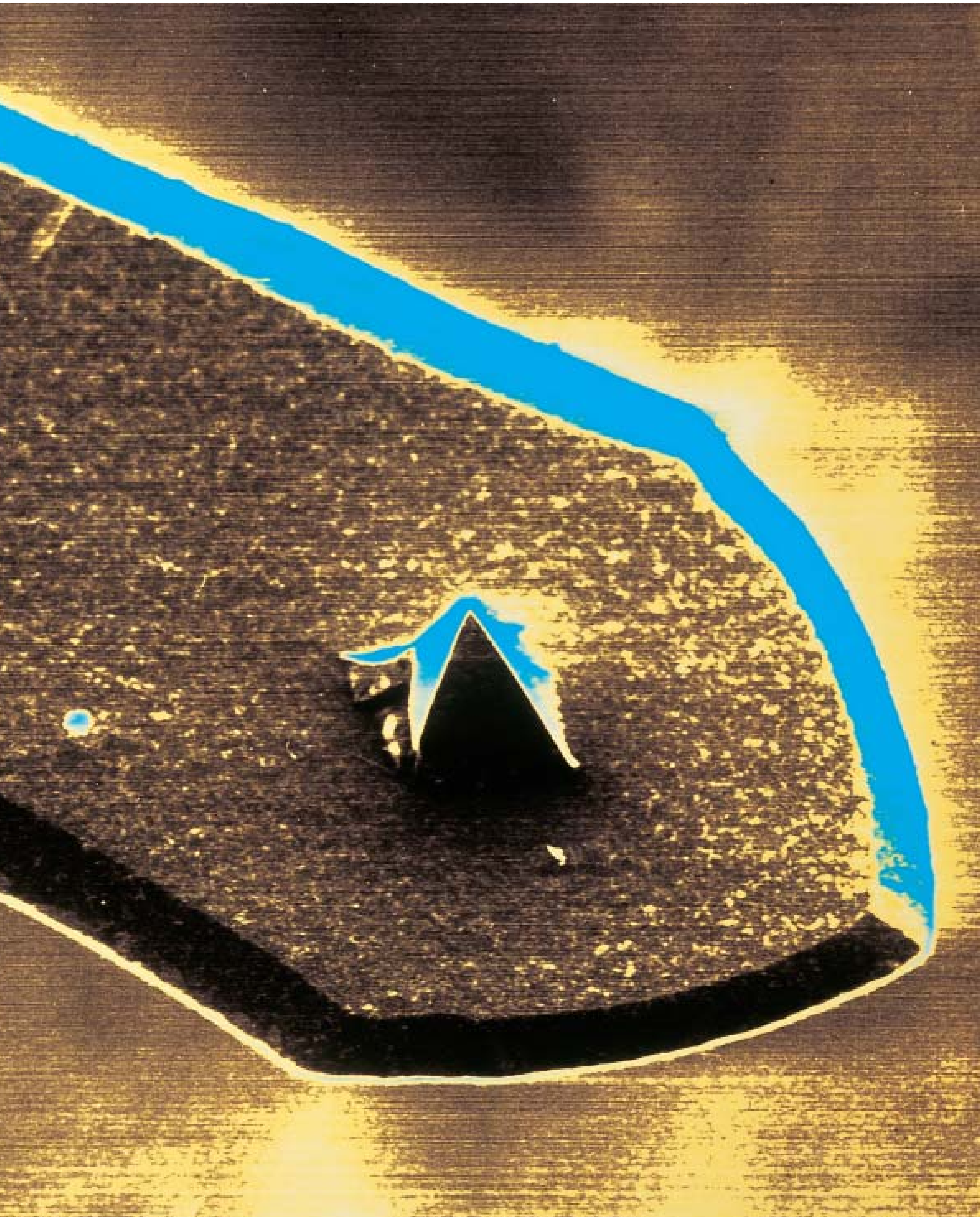
This situation represents a major challenge for research. Toxicological studies cannot simply be carried out on certain particles and the findings compulsorily applied to all other nanoparticles. Generalising from such studies must be avoided. Should every material, in principle, have its own Material Safety Data Sheet (MSDS) giving information about its toxic properties? That would entail great expense, since the commonly used testing methods provide insufficient information for binding conclusions. Ways and means must be found of permitting a proper assessment of the risk and ensuring that these new materials are handled safely.

Standardisation is essential

It is essential to have an internationally valid standardisation of nanotechnological substances and materials as well as a uniform nomenclature. Only if the various classes of substance are precisely defined and everyone is "talking about the same thing" can the results of the risk assessments of different institutions or countries be compared, thus facilitating progress in the clarification of potential risks. Without a uniform "language", neither regulative measures nor underwriting formulations ("wordings") are possible. Without standardisation, even the labelling of products becomes an extremely difficult undertaking. If there were standardisation, one might even consider the value of disclosure obligations for companies dealing with products that contain nanomaterials. These would enable insurers to recognise the presence of such products in their portfolios.

17 www.osha.eu.int

Cantilever tip manufactured entirely from a 1 µm-thin CVD diamond layer for an atomic force microscope (AFM) used to scan samples in the atomic range. Photograph taken with a scanning electron microscope (SEM).



7 Implications for insurance

The introduction of nanotechnology means a paradigm shift – both in industrial applications and in the exposure mechanisms. It is likely that in the course of its entire evolution, humankind has never been exposed to such a wide variety of substances that can penetrate the human body apparently unhindered.

How likely is it that a relationship will be established between cause and effect for potential claims caused by nanoparticles? In view of the results that are familiar to us from, for example, exposure to diesel exhaust fumes, a causal connection would appear to be perfectly possible. Presumably, one would not just identify another substance in the long list of co-carcinogens, with which people are confronted daily anyway. It is more likely that, for certain products, proving exactly where they come from, who manufactured them and what harm they have done to the claimant could be possible.

"(Nanotechnology) is going to blow the pants off Moore's Law."
Jillian Buriak, Canadian nanotech scientist and Professor and Senior Research Officer, National Institute for Nanotechnology (NINT)[18]

Revolutionary risk trend
The insurance industry is concerned, not as much because experience shows that new technological developments tend to give rise to new loss scenarios, as because the extent of these potential claims can either be difficult or impossible to assess correctly. The examples of accidents and individual claims frequently mentioned in connection with nanotechnology are only the tip of the iceberg. The errors that occur in development, design, manufacturing and information dissemination should, to some extent, be expected in all new technologies. In terms of risk and underwriting considerations, technological leaps have been known in the past: riveting was succeeded by welding, natural fibres by artificial fibres, metal by plastic, amplifier tubes by transistors, the piston by the turbine, the horse-drawn carriage by the automobile, and the electric conductor by optical cable, for example.

A solution to the problem facing information technology?

According to Moore's Law, computing capacity, or the number of transistors per chip, doubles every eighteen months. With slight deviations, this tendency has proven correct in the past. Intel's first chip (1971) had 2000 transistors[19], while today's chips operate with some 100 million. If this trend towards increased memory capacity is to continue, however, new storage technologies must be found, because the current technologies are soon going to reach the limits of miniaturisation. In order to escape this technological dead end, a technological change has to take place, such as the shift made from the switching relay to the transistor, the innovation which spurred the development of the computer in the first place.

Thus, feverish efforts are currently underway to develop a kind of nano-electronics – a technology free from the limitations of the lithography in use today. Research concentrates on nano-tube transistors, quantum processors, DNA and enzyme computers, as well as the requirements for rapid storage media.

Although these new techniques are not yet in use universally – at least on an industrial scale – nanotechnology is already regarded as the solution to a host of problems in the electronics field. The IBM "Millipede" storage medium, which operates on a nanoscale, is one of the few products that might soon reach the market. It is designed to store 25 DVDs – ie over 100 GB – on a surface area the size of a postage stamp.

18 Martin Patriquin, "Small Matter Provokes a Major Debate," *Toronto Globe and Mail* (19 November 2003)

19 J. Wolfe, "Will Nanotech Preserve Moore's Law?" *Nanotech Report*, Forbes Wolfe, ed. (September 2003)

All these technological changes were readily accepted by insurers, as little in the way of unforeseeable problems was to be feared. As far as risk was concerned, those tended to be *evolutionary* developments, with which insurance companies can generally cope – even if they do so reactively. However, the risk landscape never saw a categorically drastic change; there were no uncertainties that defied assessment, nor any real threat to risk bearers.

The situation is different in relation to developments that in terms of risk are *revolutionary,* and whose potential for damage cannot be assessed. Such developments come in two different forms: firstly, potential risks related to events attributable to a cause, and, secondly, those whose causality merely cannot be excluded, ie the so-called *phantom risks*.

Phantom risk
A phantom risk refers to a phenomenon which is perceived by the population as a threat, although no scientifically demonstrable causal connection can be established.

Nanotechnology may well belong to the category of revolutionary risks that can be shown to have harmful consequences. At the same time, the assessment of potential losses must be assumed to be either impossible or at least very difficult with regard to their scale, location and time of occurrence. What makes nanotechnology completely new from the point of view of insuring against risk is the unforeseeable nature of the risks it entails and the recurrent and cumulative losses it could lead to, given the new properties – hence different behaviour – of nanotechnologically manufactured products.

No long-term experience
In the assessment of nanotechnology, scientists have been unable to draw upon toxicological studies or long-term experience. The studies needed for purposes of risk assessment have often failed to materialise because of a lack of research funding. It is not easy to obtain financing for toxicological studies; sponsors are primarily interested in scientific progress or valuable patents. An agreed upon framework within which publicly financed projects, on the one hand, and the industry's own risk analyses, on the other, can be conducted, is direly needed.

"The role of the infinitely small is infinitely large."
Louis Pasteur

While the science of nanotechnology is still in its early stages, the insurance industry hopes that its impact will be overwhelmingly positive. We must remain vigilant, nevertheless, and pay attention to the lessons learnt from the past. One example of a product which did not develop positively was asbestos. How do we ensure that nanotechnology follows a more promising path? Years ago, asbestos enjoyed great popularity and was widely used as one of the most fire-resistant and durable substances available. Much like certain nanotechnologically manufactured products today, products containing asbestos were used in innovative ways and in many beneficial applications. What is more, asbestos fibres were not in any real sense toxic or chemically suspect. Yet their fibres could, merely on account of their form and size, cause grave harm to lung tissue – a property whose consequences were only discovered years later.

This late discovery saw regulations and protective measures being introduced only after patients all over the world had fallen incurably ill. While isolated studies had already indicated potential risks earlier, the true extent of the damage could not be foreseen even approximately in the absence of long-term experience.

"The discoverer of an art is not the best judge of the good or harm which will accrue to those who practice it."
Plato

Now society and the insurance industry are confronted with the question: what effects will nanotechnology and its products have on human beings and the environment? Most nanoparticles are presumably non-toxic in the strictest sense. In view of their diminutive size, however, they have special properties with resultant risks that are still largely unknown. And no one really wants to wait and see what the lessons of long-term experience will be.

Despite early warnings about the effects of asbestos on health, it took some 100 years to introduce internationally accepted asbestos standards; it would be advisable to find a consensus faster this time. Inasmuch as the risk environment has changed markedly between then and now, this might well be expected.

Asbestos: early warnings and measures

1898	UK Factory Inspector Lucy Deane warns of harmful and "evil" effects of asbestos dust.
1906	French factory report of 50 deaths in female asbestos textile workers and recommendation of controls.
1911	"Reasonable grounds" for suspicion, from experiments with rats, that asbestos dust is harmful.
1911 and 1917	UK Factory Department finds insufficient evidence to justify further actions.
1918	US insurers refuse to cover to asbestos workers due to assumptions about injurious conditions in the industry.
1930	UK Merewether Report finds 66% of long-term workers in Rochdale factory with asbestosis.
1931	UK Asbestos Regulations specify dust control in manufacturing only and compensation for asbestosis, but this is poorly implemented.
1935–49	Lung cancer cases reported in asbestos manufacturing workers.
1955	Doll establishes high lung cancer risk in Rochdale asbestos workers.
1959–60	Mesothelioma cancer in workers and public identified in South Africa.
1962/64	Mesothelioma cancer identified in asbestos workers, in neighbourhood "bystanders" and in relatives in the United Kingdom and the United States, among others.
1969	UK Asbestos Regulations improve controls, but ignore users and cancers.
1982–89	UK media, trade union and other pressure provokes tightening of asbestos controls on users and producers and stimulates substitutes.
1998–99	EU and France ban all forms of asbestos.
2000–01	WTO upholds EU/French bans against Canadian appeal.

Source: David Gee and Morris Greenberg, "Asbestos: from 'Magic' to Malevolent Mineral". Late Lessons from Early Warnings: The Precautionary Principle 1896–2000. EEA Environmental Issue Report, no. 22, 2001, p. 61.

7.1 Asbestos – a viable comparison?

The comparison of nanotubes with asbestos fibres has caused quite a stir. Specialist articles point out that some nanotubes are similar in form and size to asbestos fibres. The supposition that the potential for harm could be similar would appear to be obvious and is subject to discussion in expert circles.

Nanotubes, however, account for only a small part of the nanomaterials currently being produced. Even if this proportion grows larger with time, it is the much larger proportion of non-tube-shaped nanoparticles that should be subjected to minute scrutiny. The insurance industry would be well advised to follow these developments closely and familiarise itself as many applications of nanoparticles as possible.

Nanoparticles are already contained in numerous products worldwide and occur in various applications. There are indications that certain nanomaterials are potential health hazards. The danger is most probably not of an acute but of a chronic nature, and it could be some time before it manifests itself. That is where the real risk for insurers lies, and the comparison with asbestos should be seen in this light.

Asbestos analogy

Aspect	Nanotechnology	Asbestos
Manufacturer known	✓	✓
Defined substance	No	✓
Worldwide dissemination	✓	✓
Wide range of use	✓	✓
Acutely toxic	No	No
Persistent	In some cases	✓
Long-term effect	Conceivable	✓
Risks	Unknown	Cancer
Claims series potential	✓	✓
Loss accumulation potential	✓	✓
Agent analytically provable	✓	✓

Risk assessment

Risks arising out of the introduction of new products or innovative technologies need not reveal themselves immediately and may occur after an interval of years. Although this makes it no easier for the insurer to assess risks or set premiums, to do so is still possible as long as loss scenarios are conceivable and the number and extent of the resultant claims can be assessed. This is true as long as we are dealing with potential individual claims, even of a novel nature. Nanotechnology, however, is set to spread – to such a wide range of industries and in such a large number of applications and at such speed – that the individual claims conceivable on the basis of experience and resulting from the development, design, product and application defects can hardly be expected to be long delayed. Things will become critical if systemic defects only emerge over time, or if a systematic change in behaviour remains undetected for a long time. In that case, an unforeseeably large loss potential could accumulate, for example, in the field of health impairment.

An assessment of risk or loss will only be possible if and when the first health impairments have demonstrably manifested themselves. As there are indications that certain nanoparticles might only be recognised as harmful after a considerable time, the insurer must – for risk assessment purposes – know about the application areas and the dissemination of potentially suspect nanoproducts as well as about the precautionary and loss-prevention measures being taken.

In the field of occupational diseases and product liability, the risk of human and physical exposure increases the more the distance from foreign substances and potentially hazardous influences is reduced. It is greatest if harmful substances can directly penetrate the body.

If this happens without people's knowledge and in an uncontrolled manner, claims for compensation may certainly be expected in the event of health impairment. The more time passes before the harmful effect is recognised, the greater the cumulative claim for compensation will be. So if one wants to assess the potential risk in terms of scale, one must be familiar with the dissemination routes of the potentially hazardous substances. If the dissemination were limited to products with direct access to the body – ie food, personal hygiene and medication – a rough risk assessment would be possible; but if the hazard were to spread to the environment, the air and our drinking water, this would not be the case.

These channels are open to nanoparticles, at least theoretically. Furthermore, many of the artificially manufactured nanoparticles would be traceable back to the manufacturer, which would make the establishment of liability easier than in the case of substances that are universally present, such as the ultrafine particles from diesel exhaust fumes.

Therefore, if the risks of nanotechnological products are to be assessable and manageable, tests to determine their long-term toxicity are advisable. New kinds of testing and experimental methods may be required.

It will be no easy task for insurers to recognise the potential risks; both the manufacture and the use of nanomaterials are going to spread rapidly. The early application areas included pigmentations, surface treatments and coatings of all kinds. Nowadays, the manufacturers of cosmetics and household products are also using the special properties of nanotechnological substances, as are the electronics, automobile and aircraft industries. The experts agree, however, that the greatest potential benefits at present are in the fields of medicine and pharmaceuticals. In the medical field, as we have seen, nanoparticles are used to transport the active substances to specific organs. Knowledge of the potential side effects will only be amassed over time from individual cases. As regards the assessment of the product liability risk attached to such new drugs, the following principle continues to apply: the loss potential of unexpected side effects increases with the time it takes for them to manifest themselves and with the degree of market penetration. Life-style preparations are more exposed than life-preserving medicines as far as their probability of claims due to side effects is concerned.

7.2 Risk management

Insurers are going to have to live with the uncertainties of nanotechnological risks for a long time to come, meaning they will not be able to precisely determine either the probability of a loss occurring or its possible extent. This will work as long as the individual claims – following the technological development – pursue an evolutionary course, and the insurer can constantly adapt his risk management system to the changed circumstances. What must be avoided, however, is an unforeseeable, ruinous loss accumulation unleashed by a flood of late claims. As always, if the liability risk is incalculable, the insurer must limit his commitment in such a way that he can at least assess his own worst-case loss scenario. Among the most important loss-limiting measures are underwriting measures that limit the probability of a claims series. This is achieved by allocating a loss to a series or, in some cases, to an event. Allocation to an event is limited in amount and can thus be borne by the insurance industry.

"Frequent demands for absolute safety, controllability and reversibility cannot be fulfilled and represent a failure to appreciate the fact that new technologies not only solve problems but also create new ones. The less acceptance the public shows towards new risks, the less trust is placed in the means to deal with them and the greater the likelihood that the possible negative consequences of each new technology will become a problem for the insurance industry."
Swiss Re: Genetic engineering and liability insurance, The power of public perception, 1998

The "stacking of limits" problem can be avoided by means of "claims-made" cover, loss definitions and exact descriptions of the circumstances under which a loss may be said to have occurred. A claims series clause should make it possible to assign claims that gradually begin to stand out, ideally to the year in which the first loss of the series became known. The high cover required for potential exposure to a claims series should be exclusively achieved by appropriately defining the cover periods and, where applicable, setting high limits.

Cover that permits "fear of claims" should not be granted. Moreover, the conditions governing loss reporting should allow for the fact that a claims series could arise.

7.3 A challenge for risk communication

Often unclear to the layperson is what nanotechnology actually is, what special qualities nanoproducts may have, and what the possible risks are. For the approach is not just a question of an extremely multifaceted technology; the manufacturing processes and operating mechanisms of nanotechnological products remain largely inscrutable to observers, users and consumers. This may lead to uncertainty and scepticism in society at large, especially if the various risk aspects become the subject of public discussion.

In contrast to the debates on nuclear power and genetic engineering, the public does not yet view nanotechnology as a noteworthy threat. Many, in fact, are still quite unaware of its introduction. The increase in media interest since the beginning of 2003 could change this situation, however, and lead to more lively debate on nanotechnology's benefits and risks. Whether the public accepts the new technology and sees in it advantages for itself – or rejects it – will largely depend on how well informed it is and to what degree it is able to make objective judgments.

"Public issues"
These are concerns voiced by pressure groups, which pass through the stages of published and public opinion to become political issues. Once on the political agenda, their incorporation into legislation is only a question of time.

"In the absence of good evidence that today's exposures to carcinogens are safe, it is wiser to apply the precautionary principle, and assume they are unsafe, especially if the disease (or ecological impacts) from higher exposures have no known threshold of exposure below which there are no effects."
David Gee and Morris Greenberg[20]

No question, however: nanotechnology will sooner or later emerge as a *public issue*. Ever since genetic engineering entered the public consciousness, it has become obvious that the protest of society can brake the further development of a new technology. Consequently, it must be in the interest of industry to take the misgivings and needs of society seriously and make allowance for them in subsequent stages of development.

The consumer is exposed to the influence of reams of information, some of it contradictory. He not only hears the good news about product innovation, but also the warnings and consumer misgivings. Talking openly and responsibly about risks is the task of all those who possess the necessary knowledge and, above all, of those in the manufacturing industry. Dialogue is needed among science, industry, the authorities and the public. As the risk carrier, the insurer carries the responsibility for leading the risk dialogue, including with lawmakers.

7.4 A lesson learnt

Once a certain opinion has become socially established, it is an extremely difficult, tedious and costly undertaking to persuade people of the contrary. Instead, the public must realise from the outset that a new technology not only solves problems, but also creates them, which, in turn, can lead to the emergence of new risks.

How people assess risks depends on a whole series of subjective perceptions. The so-called "fright factors" (see text box, page 46) tell us whether an issue has the potential to create panic and hence is perceived as a threat. These factors include the origin of a risk. Is it a new man-made technology and hence a "homemade problem", or is it a natural occurrence with which people have contended for generations? If the anticipated damage turns out to be irreversible, that fact itself will generate far more fear than if people believe that countermeasures can be taken.

Fear is also aroused by those risks that are forced upon the consumer, in which case, he cannot take an independent decision. This underscores the importance of the product declaration, which enables the consumer either to accept a risk voluntarily or reject it.

The risk itself is hard to assess scientifically and is the subject of much dispute in research circles. Above all, contradictory statements made by scientists, on the one hand, and by the authorities, on the other, generate public mistrust. Fears are also reinforced by controversial statements made by experts on the subject of risks.

20 David Gee and Morris Greenberg, "Asbestos: from 'Magic' to Malevolent Mineral." *Late Lessons from Early Warnings: The Precautionary Principle 1896–2000.* EEA Environmental Issue Report, no. 22 (2001): pp. 52–63.

Fright factors

Why do some risks trigger so much more alarm, anxiety or outrage than others, seemingly regardless of scientific estimates of their seriousness? Research over many years in the so-called "psychometric" tradition (Fischhoff et al. 1978, 1991; Slovic 1986; Gardner and Gould 1989) has sought to find answers to this key question. Some fairly well-established rules of thumb have emerged.

Risks are generally more worrying (and less acceptable) if perceived:

1. To be involuntary (eg exposure to pollution) rather than voluntary (eg dangerous sports or smoking).
2. As inequitably distributed (some benefit while others suffer the consequences).
3. As inescapable by taking personal precautions.
4. To arise from an unfamiliar or novel source.
5. To result from man-made, rather than natural sources.
6. To cause hidden and irreversible damage, eg through onset of illness many years after exposure.
7. To pose some particular danger to small children or pregnant women or more generally to further generations.
8. To threaten a form of death (illness/injury) arousing particular dread.
9. To damage identifiable rather than anonymous victims.
10. To be poorly understood by science.
11. As subject to contradictory statements from responsible sources (or, even worse, from the same source).

By permission of Oxford University Press[21]

There has been disagreement among scientists on the question of what the most important factor for the potential toxicity of nanoparticles might be. The answers tend to be contradictory. This leads to a decline in confidence, as the controversy over the risks of BSE in the early 1990s clearly demonstrated.

The public perspective
What will society decide with regard to the spread of nanotechnology? Will it support it because it expects the technology to yield a number of definite advantages? Or will it take a sceptical view of its further development, given that the question regarding possible risks has not been satisfactorily answered?

Up to now, little has been heard from the public on this subject. Too few people are aware of developments in the field of nanotechnology, and fewer still have formed an opinion. Even the word "nanotechnology" is still unknown to many, for whom neither a "positive" nor a "negative" image is associated with the term "nano". That, of course, is a state of affairs that can change quickly. A media event on the subject of nanotechnology or a negatively perceived occurrence related to a nanotechnologically manufactured product can shake the public's critical consciousness awake.

In his bestseller, *Prey*, Michael Crichton – author of *Jurassic Park* – describes a horror scenario of the world nearly coming to an end as a result of the improper application of nanotechnology. The proliferation of intelligent nanoparticles is out of control. Fact and fiction are so inextricably bound that the reader with no previous knowledge of the subject is hard put to distinguish between them. He or she never learns that the whole field of Artificial Intelligence and "self-assembly" is still far from any kind of practical application – assuming it will ever be possible. That reader (and cinemagoer) will probably associate nanotechnology with Artificial Intelligence and menacing scenarios from now on.

21 Peter Bennett and Kenneth Calman, *Risk Communication and Public Health* (Oxford: Oxford University Press, 1999), p. 6.

7.5 The precautionary principle

The responsible authorities face the task of ensuring the safe handling of nanotechnological products and applicators as regards their rapid dissemination in society. Without sound scientific knowledge of the risks involved, however, this is hardly possible under current law.

A sensible pursuit of technological research and development, on the one hand, while offering people and the environment the best possible protection against possible hazards, on the other, must be found. This challenge has prevented the introduction of the precautionary principle in relation to new technologies for more than 20 years. The precautionary principle demands the proactive introduction of protective measures in the face of possible risks, which science at present – in the absence of knowledge – can neither confirm nor reject.

This "better safe than sorry" approach prescribes that necessary measures to protect people and the environment should be introduced at an early stage, even if the scientific uncertainties regarding the risks have not yet been finally clarified. The Rio Convention of 1992 states: *"Where there are threats of serious or irreversible damage, lack of scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation".*[22]

Whether and at what stage of development such measures should be adopted is equally difficult to determine. While one does not want to take costly protective measures that are not needed – especially if they might have a negative effect on continuing economic development – neither people nor the environment ought to be burdened with dangers that could have been avoided.

The dilemma surrounding the precautionary principle is at present the subject of a number of public discussions – especially the one dealing with mobile communication or genetically modified foodstuffs. To date, despite all efforts at the international level, no precautionary principle has been agreed upon to satisfy all the parties involved, because the details of the situation on which a decision had to be taken differed so radically.

In view of the dangers to society that could arise out of the establishment of nanotechnology, and given the uncertainty currently prevailing in scientific circles, the precautionary principle should be applied whatever the difficulties. The handling of nanotechnologically manufactured substances should be carefully assessed and accompanied by appropriate protective measures. This is particularly important for individuals whose jobs expose them to nanoparticles on a regular basis. At the same time, no reasonable expense should be spared in clarifying the current uncertainties associated with nanotechnological risks.

22 Rio Convention, United Nations Conference on Environment and Development: "Rio Declaration on Environment and Development" (14 June 1992) *International Legal Matters 31:* pp. 874–879.

The main precondition for successful risk assessment in a technology as complex as nanotechnology is finding a consensus among industry representatives, legislators and research institutes concerned. It is one which must extend across national borders. Only if the many open questions are addressed in an organised way can the attempt to analyse the risks be successful.

The burden of research work must be shared by several parties. Neither industrial companies nor public institutions are able to acquire sufficient capacity to investigate these questions on their own. Although some individual institutions and companies are already conducting their own risk analyses and financing them parallel to product development, it cannot be the task of any individual company to bear the burden of the certificate of non-objection alone. Furthermore, the efforts of individuals are hardly going to be enough to obtain a comprehensive picture of the risk landscape. A certain degree of standardisation and a basic framework, starting with the nomenclature, are prerequisite to improving the co-ordination of these efforts.

Certain certificates of non-objection and long-term studies should be given legal status and distributed among various research institutes with appropriate research funding. Industry must also make its contribution by taking an active part in risk research and raising public awareness of risk.

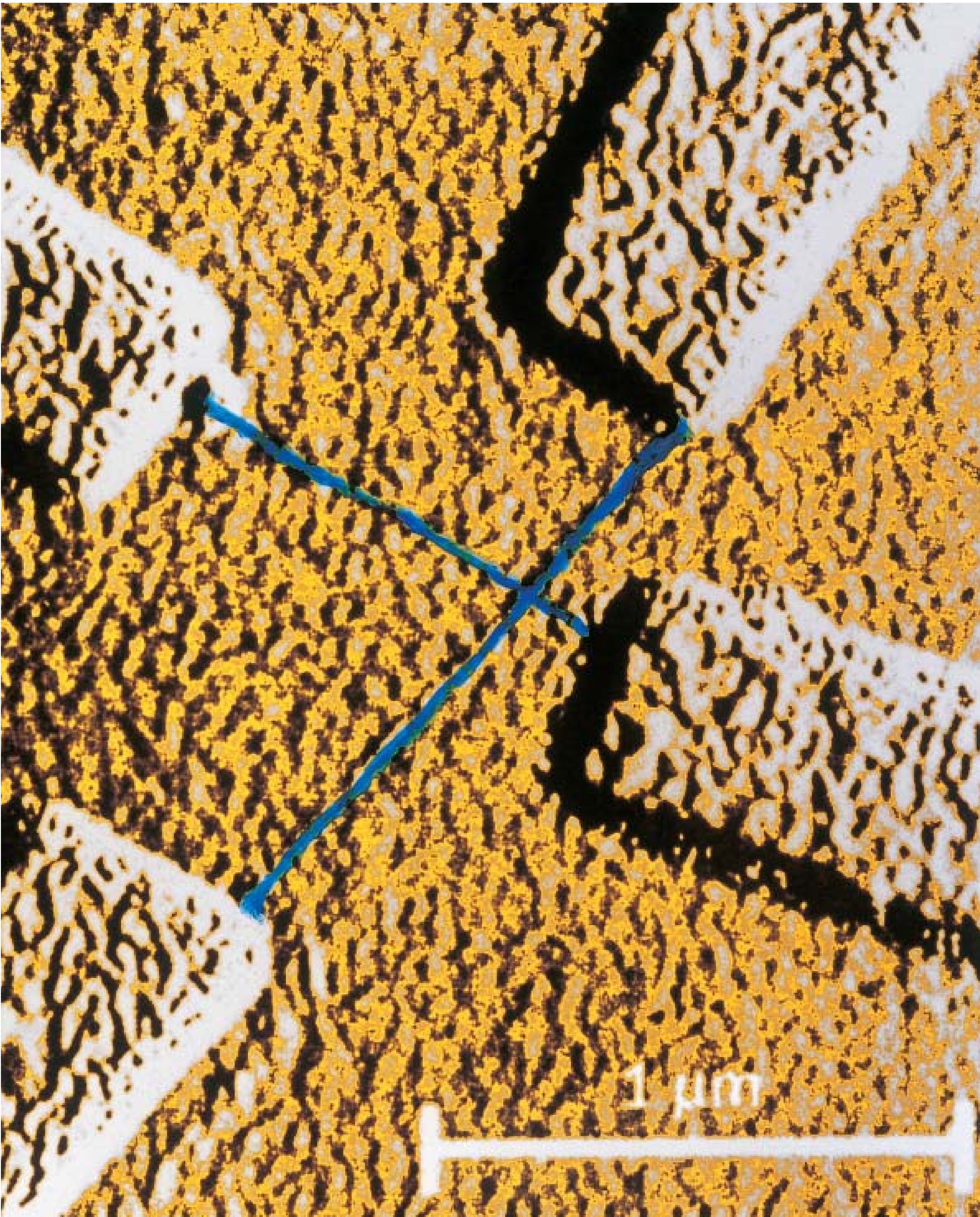
7.6 Fostering partnership

The insurance industry has the task of assuming the uncertainties and risks of its business partners. In the case of new technologies, the uncertainties prevail, since neither the probability nor the extent of the potential losses are precisely calculable. This is in contrast to the large number of familiar risks in an insurance portfolio, which can be reduced to numerical terms on the basis of experience.

By providing cover for uncertainties – more specifically, by facilitating or enabling a launch into ventures involving risk – the insurance industry makes a key contribution towards technical progress. To be an effective and competent partner for industry, however, it must focus upon identifying, analysing and measuring risks, so that assuming them does not present unpleasant surprises. Making risks assessable and calculable is the insurers' strength; a strength from which everyone benefits. In this, however, it must pool its knowledge and engage in dialogue with all the representatives of a community bound together by a shared risk.

Only those who have a clear picture of the risk landscape can be reliable partners in the risk business itself.

Two intersecting transistors seen through the atomic force microscope (AFM) on a scale of 1 μm.



Appendices

Appendix 1: Summary of application areas for information technology

Material/technique	Applications	Time-scale (to market launch)
Pre-2015		
Quantum well structures (pers. comm., Gareth Barry, Imperial College London, 22 Nov 2002)	Telecommunications/optics industry. Potentially very important applications in laser development for the data communications sector.	Quantum well lasers already utilised in CD players. Not yet optimised for the communications market (ie fibre optics): 4–5 years.
Quantum dot structures (source as above)	The aim is to use fibre optic communication in building and computers. The problems are cost and high temperature operating conditions. Quantum well/dot structures can potentially solve this problem.	Quantum dots still in research stage: 7–8 years.
Photonic crystal technologies (Miles and Jarvis 2001)	Optical communication sector, ie fibre optics. Photonic integrated circuits can be nearly a million times denser than electronic ones. Their tighter confinement and novel dispersion properties also open up opportunities for very low power devices.	Still in basic R&D, but very strong commercial interest emerging.
Carbon nanotubes in nanoelectronics. These hold promise as basic components for nanoelectronics – they can act as conductors, semiconductors and insulators (Holister, 2002)	Memory and storage; commercial prototype nanotube-based (non-volatile); RAM; display technologies; E-paper.	Commercial prototype nanotube-based RAM predicted in 1–2 years. Consumer flat screen by the end of 2003. Limited commercialisation of E-paper in 1–2 years.
Spintronics – the utilisation of electron spin for significantly enhanced or fundamentally new device functionality (Science Blog, 2002)	Ultra-high capacity disk drives and computer memories.	A read head has been demonstrated that can deal with storage densities of a terabit per square inch. In 2001, Fuji announced a new magnetic coating promising a 3-gigabyte floppy disk.
Polymers (Compano, 2001)	Display technologies – this sector is driven by the electronics consumer market.	Some commercialisation, eg Cambridge Display Technologies, has been formed specifically to exploit this technology.
Post-2015		
Molecular nanoelectronics (including DNA computing) (Compano, 2001)	Circuits based on single molecule and single electron transistors will appear, initially in special applications.	Single atom transistor demonstrated recently. Still immature, but huge potential (Miles and Jarvis, 2001).
Quantum information processing (QIP) (Compano, 2001)	Several researchers have devised algorithms for problems that are very computationally intensive (and thus time-consuming) for existing digital computers, which could be made much faster using the physics of quantum computers, eg factoring large numbers (essential for cryptographic applications), searching large databases, pattern matching, simulation of molecular and quantum phenomena (Anton et al., 2001).	Still in pure research phase, although some US defence money has been made available (Holister, 2002).

Source: Greenpeace Environmental Trust, "Future Technologies, Today's Choices." July 2003, page 26.

Appendix 2: Summary of application areas for nanoscale pharmaceuticals and medicine

Material/technique	Property	Applications	Time-scale (to market launch)
Diagnostics			
Nanosized markers ie the attachment of nanoparticles to molecules of interest (Holister, 2002)	Minute quantities of a substance can be detected, down to individual molecules.	eg detection of cancer cells allows early treatment.	?
"Lab-on-a-chip" technologies (Saxl, 2000)	Miniaturisation and speeding up of the analytical process.	The creation of miniature, portable diagnostic laboratories for uses in the food, pharmaceutical and chemical industries; in disease prevention and control; and in environmental monitoring	Although chips currently cost over GBP 1250 (USD 2085) each to make, within three years the costs should fall dramatically, making these tools widely available.
Quantum dots (pers. comm., Gareth Barry, Imperial College London, 22 Nov 2002)	Quantum dots can be tracked very precisely when molecules are "bar coded" by their unique light spectrum.	Diagnosis	In early stage of development, but there is enough interest here for some commercialisation (eg Q-dot-Inc.).
Drug delivery			
Nanoparticles in the range of 50–100 nm (Miles and Jarvis, 2001)	Larger particles cannot enter tumour pores while nanoparticles can easily move into a tumour.	Cancer treatment	?
Nanosizing in the range of 100– 200 nm (Miles and Jarvis, 2001)	Low solubility	More effective treatment with existing drugs	?
Polymers (Holister, 2002)	These molecules can be engineered to a high degree of accuracy.	Nanobiological drug carrying devices	?
Ligands on a nanoparticle surface (Holister, 2002)	These molecules can be engineered to a high degree of accuracy.	The ligand target receptors can recognise damaged tissue, attach to it and release a therapeutic drug.	?
Nanocapsules (Holister, 2002)	Evading body's immune system while directing a therapeutic agent to the desired site.	A Buckyball-based AIDS treatment is just about to enter clinical trials (Ho, 2002a).	Early clinical
Increased particle adhesion (Holister, 2002)	Degree of localised drug retention increased.	Slow drug release	?
Nanoporous materials (Holister, 2002)	Evading body's immune system while directing a therapeutic agent to the desired site	When coupled to sensors, drug-delivering implants could be developed.	Pre-clinical: an insulin-delivery system is being tested in mice
"Pharmacy-on-a-chip" (Saxl, 2000)	Monitor conditions and act as an artificial means of regulating and maintaining the body's own hormonal balance	eg diabetes treatment	More distant than "lab-on-a-chip" technologies
Sorting biomolecules (Holister, 2002)	Nanopores and membranes are capable of sorting, for example, left and right-handed versions of molecules.	Gene analysis and sequencing	Current –?
Tissue regeneration, growth and repair			
Nanoengineered prosthetics (Miles and Jarvis, 2001)	Increased miniaturisation; increased prosthetic strength and weight reduction; improved biocompatibility	Retinal, auditory, spinal and cranial implants	Most immediate will be external tissue grafts; dental and bone replacements; internal tissue implants (Miles and Jarvis, 2001).
Cellular manipulation (Miles and Jarvis, 2001)	Manipulation and coercion of cellular systems	Persuasion of lost nerve tissue to grow; growth of body parts	More distant: 5–7 years

Source: Greenpeace Environmental Trust, "Future Technologies, Today's Choices." July 2003, page 28.

Appendix 3: Summary of application for energy processing

Material/techniques	Applications	Time-scale (to market launch)
Power generation (PV technology)		
Polymer materials (organic)	Solar cells (pers. comm., Jenny Nelson, Imperial College London, 2 Dec 2002). Current developments aim to balance moderate efficiency with low cost. Another big advantage is that these layers can easily be incorporated into appliances. Current problems stem from the material's instability.	The research stage has advanced much more quickly than expected. As a result, polymer-based PV cells should enter the market in 5 years.
Combinations of organic and inorganic molecules	Dye-sensitised solar cells made from a thin hybrid layer (pers. comm., Jenny Nelson, Imperial College London, 2 Dec 2002). These cells are potentially very cheap because fabrication is from cheap, low purity materials by simple and low cost procedures (Saxl, 2000). Photocatalytic water treatment.	Low power applications will enter market first. Limited commercialisation already occurring (eg by Sustainable Technologies International)
Quantum wells (inorganic)	Quantum-well solar cells (pers. comm., Jenny Nelson, Imperial College London, 2 Dec 2002). Current research is taking place in high-efficiency applications because the infrared part of the solar spectrum may be absorbed.	Pure research
Nanorods	These structures can be tuned to respond to different wavelengths of light forming cheap and efficient solar cells (Holister, 2002).	Long-term
Fuel conversion/storage		
Improved fuel catalysts through nanostructuring	Fuel conversion (Saxl, 2000).	Current – 3 years
Nanotubes	Fuel storage, eg a methane-based fuel cell for powering mobile phones and laptops, is currently being developed (Holister, 2002).	2 years
Nanoparticles	Vastly increased (eg x 10) charge and discharge battery rate (Holister, 2002)	Distant

Source: Greenpeace Environmental Trust, "Future Technologies, Today's Choices." July 2003, page 29.

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