

Michael Steinfeldt (Editor)

# Nanotechnology and Sustainability

Prospective Assessment of a Future Key Technology

Schriftenreihe des IÖW 167/03



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INSTITUTE FOR  
ECOLOGICAL ECONOMY RESEARCH



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Prospective Assessment of a Future Key Technology

With contributions from Ulrich Petschow, Dr Arnim von Gleich and Dr Silvia Diabaté

In Cooperation with: a research project funded by the German Federal Ministry for Education and Research, Bonn (Fkz: 16/1504)

Schriftenreihe des IÖW 167/03  
Berlin, September 2003

ISBN 3-932092-68-6

# Imprint

Publishers:

Institut für ökologische

Wirtschaftsforschung (IÖW)

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*Economy Research*

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New Edition 2009

## Abstract

This paper presents the current state of knowledge within our project - funded by the German Federal Ministry of Education and Research – dealing with the effects of the production and application of nanotechnological products on sustainability. It also considers suggestions made at an experts' workshop held in Berlin on the 16th of January 2003. This publication is rather intended to contribute to the ongoing discussion on the innovation analysis and technical assessment of nanotechnologies than to be a final project report.

The various contributions deal with different aspects of prospective technology assessment in the field of nanotechnology. Topics include: guiding principles as an aid to orientation and a means of shaping technologies; the "characterization of technologies" as both a generalized approach towards technology assessment and a conceptual framework for assessing actual nanotechnology applications. We review the state of the art concerning the safety of nanotechnology and its impact on the environment and health; a contribution on the toxicology of nanoparticles is also included.

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# Introduction

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Nanotechnology holds a prominent position in current research and technology policy. The huge potential for innovation and the attendant economic opportunities are resulting, on a world-wide scale, in more and better-funded research programmes in this field. It is not, however, possible to make 'predictions' about specific technological developments or about their economic, ecological and social impacts.

There is, therefore, a need for debate on the effects of innovation and technology, and on the impact of nanotechnology on sustainability. We have seen a recent intensification of such discourse, largely as a result of the Federal Ministry of Education and Research's invitation of tenders - issued in spring 2002 - for an "innovation and technology analysis of nanotechnology". Since September 2002 three projects have been pursued in this connection:

- The economic potential of nanotechnology  
Being undertaken by: VDI Future Technologies Consulting, Düsseldorf; Deutsche Bank Micro-technology Innovation Team, Berlin
- Nanotechnology and health  
Being undertaken by: Aachen Centre of Excellence for Medical Technology (AKM), Institute for Health and Social Research, Berlin (IGES), and others
- Effects on sustainability of the production and application of nanotechnological products  
Being undertaken by: Institute for Ecological Economy Research (IOEW) in co-operation with the University of Bremen, asmec i.G. and Nanosolutions GmbH.

The papers in this publication refer to the last of the above-mentioned projects.

Entitled "The effects on sustainability of the manufacture and application of nanotechnological products", the project takes as its starting point the current state of the art in materials and technology assessment and attempts to develop this body of experience more along the lines of integrated sustainability assessment. The emphasis is on the ecological opportunities and risks of this developing technology. The complexity of the task requires that the project design incorporates at least a two-step analysis and assessment procedure:

- a. Firstly, nanotechnologies are evaluated on a general basis, in line with the concept of sustainable development, underlain by characterization of the technology
- b. Secondly, actual contexts for application of specified technologies are appraised.

A further aim of the project is to sound out (political?) means of shaping the technology to enhance its sustainability.

Within the auspices of the project, and under the heading "Nanotechnology as a means towards sustainability? Prospective assessment of a future key technology" a workshop was held in Berlin on the 16th of January 2003, at which 25 research and business experts discussed a number of issues surrounding prospective technology assessment within this field. The project team presented the various approaches to assessment it had thus developed so far, and possible case studies for

application were put up for discussion. A number of contributions by experts provided valuable input: "Release of nanoparticles through nanotechnologies with special emphasis on exposure in the workplace" by Professor H. Fissan, University of Duisburg-Essen; "Toxicology of nanoparticles" by Dr S. Diabaté, Karlsruhe Research Centre; and "Areas of nanotechnology with a high degree of market relevance" by Dr W. Luther and Dr N. Malanowski, VDI Future Technologies Consulting, Düsseldorf.

Taking into account the discussions at the workshop, the following contributions describe the current state of knowledge within the project with regard to various aspects of prospective technology assessment in the field of nanotechnology.

In the first contribution, Arnim von Gleich discusses so-called guiding principles as both an aid to orientation and a policy instrument in shaping nanotechnology along the lines of sustainability. He also puts up for discussion three specific guiding principles.

In the next chapter, he outlines the "characterization of technologies" as a generalized approach to technology assessment and applies it to nanotechnology.

The contribution by Ulrich Petschow reviews the current state of knowledge regarding the safety and the environmental and health impact of nanotechnologies.

In his paper, Michael Steinfeldt develops and applies a concept for assessing specific nanotechnology applications.

The final contribution is an essay by Silvia Diabaté of the Institute of Toxicology und Genetics at the Forschungszentrum Karlsruhe, in which the toxicology of nanoparticles is outlined in some depth.

Against the background of the presentation of the preliminary project results, we would like this publication to be taken as a contribution to the ongoing public discussion on the innovation and technology analysis of nanotechnology, and not as a final project document. Readers are welcome to comment on the contributions and to discuss their views with the authors.

# Towards sustainable nanotechnology?

## Guiding principles as a means of shaping this technology

Professor Arnim von Gleich, Faculty of Production Engineering and Technology, University of Bremen (special field: technology design and development)

### 1 Means of influencing technological development

In order to successfully influence the way in which technologies take shape and develop, it is essential that we have an adequate understanding of the processes of technological development and innovation, and the differences between them. For some time now, research on technology emergence (see, for example, Dierkes 1997) and on innovation (see, for example, Sauer; Lang 1999 / Hübner 2002) has been enhancing our understanding of the origins and development of technologies and innovations. Here, an innovation is seen as an idea that has been implemented and has proved successful in social and/or economic terms, whereas technology is regarded not only as an artefact but also as a 'social construct', the interim result of innovation processes.

Generally speaking, if an innovation is to be successfully realized this involves a highly complex network of participants (actors), the so-called 'innovation system'<sup>1</sup>. Various types can be distinguished, as can different levels of action and communication, so that innovation systems may for example be corporate, regional, national or international. Within these systems, all participants use the specific means of influence at their disposal; these vary in scale, but are generally quite limited. It is rather unlikely that a single actor or group of actors can single-handedly control the entire process of technology emergence or innovation within a given system. The probability that such innovation systems could be controlled "externally", as it were, is surely even lower.

If attempts at shaping technologies are to have any chance of success, they need to take into account the type of system involved, the spatial level at which action is desired, and the time structure of the innovation process<sup>2</sup>. Not so long ago, the history of technology was described as a process of continuous improvement, as a more or less autonomous developmental progression. And there are, indeed, phases that fit this description fairly well: at times, technological development exhibits

1 See Nelson (1993) / Freeman (1995); researchers in the field of 'generation of technology' also refer to "technology emergence networks".

2 Attempts at characterization, guided by case studies, are currently underway by the author within the SUBCHEM project being carried out by riw (the BMBF-funded innovation research program) ([www.subchem.de](http://www.subchem.de) and Hemmelskamp (2001)). The purpose of the project is to come up with design options for workable innovation systems aimed at successfully substituting hazardous substances. The significance and usefulness of windows of opportunity are the subject of the SUSTIME project: "Innovation, time and sustainability – time strategies in ecological innovation policy".

considerable “inner momentum”. During such periods it evolves – this, admittedly, being only one of a multitude of explanations put forward - in small steps, along so-called “technology paths” or trajectories. In such cases, the “direction” which development takes is largely determined by the trajectory. It is particularly difficult to change course or embrace alternatives. In this model, real chances of (successfully) influencing the course taken by the technology are restricted to specific phases (or windows of opportunity) before the system settles into a new path and/or as the system approaches an inherently necessary change of trajectory. Before the system enters a new trajectory - in other words, ahead of a new ‘technological lock-in’ – successive decisions need to be made, at every conceivable potential “fork” in the path, concerning which course to take. This situation is characterized by a high degree of freedom of action. Once a technology is newly embarked on a given trajectory, however, the options are again very limited. Opportunities to change trajectory emerge only when problems accumulate for which the existing trajectory offers no apparent solutions, or when a competing route materializes<sup>3</sup>.

However, such windows of opportunity do not open up and close again only in connection with a technology's inner dynamic. Regulatory frameworks and - especially with regard to capital goods, - phenomena such as companies' investment cycles play an important role, too.

We talk about influencing and shaping the way in which technology develops, not controlling technology as such. Any attempt at the latter (especially by “political actors” who are not otherwise directly involved) seems not only somewhat futile in the light of the complexity of the processes involved in technology emergence and innovation, but even “dysfunctional” and counterproductive. Such remarks are not intended to challenge the much-referred-to “primacy of policy” in technological development - an area which exerts a considerable and increasing influence on the living conditions of people in modern industrial societies. Neither are they meant to legitimize technocracy and “expertocracy”. Nevertheless, policy makers and others with democratic (participatory) influence should not insist on “control”. Rather - and this strategy is widely adopted - they should define and enforce guidelines and so-called “crash-barriers”, establishing explicit boundaries within which entrepreneurial activities are relatively free to “move”, while also addressing the numerous options open to actors within innovation systems (participatory micro-policy). And, not least, governmental R&D grants offer a further means by which the “undesirable” can be rejected and the “desirable” encouraged.

What we are talking about, then, are “softer” forms of influence, in keeping with the complexity of innovation processes and the partial autonomy of social sub-systems. Research in technology emergence has also demonstrated that guiding principles are an important element of these “soft forms”. If it were possible, by means of guiding principles, to intentionally influence the processes of technology emergence and innovation within nanotechnology, then this field of technology would to some extent be opened to “public and democratic discourse”.

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3 The “model” being used here in an attempt to explain the development of innovations and technologies (see in particular Dosi 1982 and 1988) has strong similarities with that of Thomas Kuhn for history of science. Kuhn posited the following stages in attempting to explain paradigm-driven scientific advancement: a) paradigm development; followed by b) “normal science” within the framework of the paradigm, then c) the amassing of problems that are insoluble within the confines of the paradigm; and finally d) onset of the paradigm shift phase, i.e. “revolutionary science” (see Kuhn 1976).

## 2 Orientation in technology design through guiding principles

Innovations are the interim results of a constant process of search and selection aimed at finding what is - for the time being, at least – the “superior solution”. The biological process of evolution would seem a fitting analogy by which to illustrate this, with its key elements of mutation/variation (creation of something new), selection (survival of the fittest<sup>4</sup>) and isolation (protected zones<sup>5</sup>). Insofar as this comparison is valid, it implies (for example) that it is critical to generate many alternatives from which to choose, and that sometimes innovations depend -at least for a time - on the existence of special or even “protected” zones.

But these analogies should not be carried too far<sup>6</sup>. After all, the evolutionary model lacks an essential aspect of human behaviour, i.e. a pursued goal. Unlike with biological species, the very survival (or even self-reproduction) of technological artefacts cannot be postulated as the “reason for” or “logic of” the process of “technological evolution”. Despite all the problems inherent in distinguishing between means and ends<sup>7</sup>, successful technological innovations usually involve combining the feasible with the desirable, i.e. coupling (often new) technical possibilities with the needs - either present-day requirements previously unmet, or future needs - or problems of society. However, combining the desirable with the feasible is a specific aspect – indeed, one of the key functions - of guiding principles<sup>8</sup>.

### 2.1 Guiding principles as 'instruments' of control in technology development

Guiding principles do influence technological development and can perhaps be used to intentionally exert an influence on technological development. They help to “orientate” innovations; they have a coordinating and synchronizing function within complex innovation systems (or technology emergence networks). Guiding principles reduce complexity, focus perception, motivate and, quite

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- 4 The double meaning of the word “fit”, which implies both “good performance” (fitness) and being “well-adapted”, is important here in relation to both the actors and their environment.
  - 5 A possible analogy from innovation research is that of the so-called “lead markets” (see a further project by the riw program: LEAD MARKET: political model of the development of international markets for innovation in sustainable economic development – from pilot market to lead market; see also Hemmelskamp 2001)
  - 6 Historically speaking, they are based on a couple of conceptual transfers (which took place during the time of Darwin and Spencer) of many aspects of the “competition” model, borrowed from the context of the market-place and applied to evolution and the origin of species.
  - 7 Strictly speaking, not the “distinction” is the problem but the attempt at “separation”, leading to the conviction that one can differentiate between “pure means” and “pure ends”.
  - 8 Here, incidentally, reference is made to a further interesting parallel with regard to the distinction between the « feasible » and the « desirable » in the debate on guiding principles. It concerns the differentiation between (or characterization of) innovations as « technology-push » and « demand-pull ». In both types - i.e. both in technical advances and in the emergence and formulation of societal needs and problems to be solved - guiding principles play an important role.

often, also lend legitimacy. They are probably of greatest importance with regard to fundamental innovations, i.e. in the phases prior to a “technological lock-in” on a new trajectory or in times of radical upheaval of problems on old paths, when new technologies open the possibility for a new trajectory.

The basic effectiveness of guiding principles can hardly be called into question, although empirical proof of how they work in detail is rare and is quite probably difficult to obtain. Less clear is the issue of whether and how guiding principles can be used “deliberately” and, in effect, “instrumentally”, in order to influence or shape technologies (e.g. Mambrey et al. 1995 / Hellige 1996 / Meyer-Krahmer 1997 / Kowol 1998). “Management by guiding principles” is one of a host of “management by” approaches reported in the literature on corporate strategic management as being comparatively successful (Bea; Haas 2001 / Matje 1996 / Blättel-Mink 1997 / KPMG 1999).

Those who wish to employ guiding principles as a means of influencing and shaping technologies need to understand what makes a successful guiding principle and how such conceptual models operate. We actually know that guiding principles work by motivating, by constituting a group identity, by coordinating and synchronizing the activities of individual actors, by reducing complexity and structuring perception. If they are to be effective, among their most important requirements are graphic quality and emotional content, in short, their capacity to resonate with the consciousness of the actors concerned<sup>9</sup>.

Three elements would appear to be of central importance: a) their pictorial quality; b) their guiding function; and c) that they are grounded within the realms of the feasible. Pictorial quality is very important in ensuring orientation and clearness and an associated reduction in complexity. The guiding function relies on emotional and value content, providing both motivation and orientation. And they need to be in touch with reality, in order that the line can be drawn between pragmatism on the one hand and utopias and visions on the other. Guiding principles should not, therefore, be too abstract in nature. Starting points for putting these maxims both into concrete form and into operation should be immediately apparent. “Sustainable economic development”, for instance, appears to be too complex, too abstract and too defensive a notion to serve as a useful guiding principle. At least within the central debate, as launched in Rio (with the combined issues of the environment, justice, climate protection, biodiversity and protection of resources), pursuit of the goal of sustainability overemphasizes mere survival (resource availability, carrying capacity) at the expense of the ‘good life’. It is probably more effective to draw up guiding principles for each specific area of need, such as “sustainable building and habitation”, as outlined and partially implemented by the 13th Enquete Commission - set up by the German parliament - on “protection of man and the environment” (see Enquete Commission, 1997). Central guiding concepts much discussed at the strategic level, such as resource efficiency, sufficiency, consistency (between natural and societal metabolisms) are also certainly too abstract. Examples of efficient, technology-oriented guiding principles at the middle level of operationalization and concretization, on the other hand, may include closed-loop recycling management, bionics (with nature as a role model) and perhaps - more recently, and especially in the English-speaking world - “green chemistry”.

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9 Here, too, are numerous striking overlaps between the concept of the guiding principle and that of the paradigm (see Kuhn 1975), especially with regard to “vividness”, “structuring of perception”, “motivation”, “creation of a group identity”, “coordination and synchronization”, “relation to feasibility” and “preferred instruments and optimal solutions”.

## 2.2 Shaping technology by means of guiding principles: a risk- minimizing strategy?

Risk minimization, especially in the light of “new technologies” and their associated (and at least partially unknown) risks, has to deal with a host of problems relating to information and prediction. How can we gauge and minimize risks that are still unknown to us? One approach to risk minimization - and to implementing the oft-demanded “precautionary principle” (this *Vorsorgeprinzip* being one of the cornerstones of German environmental law) could be that of precaution-oriented technology design. In itself, this is nothing new. The construction of technical systems on the basis of the (guiding?) principle of inherent safety has a fairly long-standing tradition in fields such as nuclear technology and chemical process technology. Here, however, comparatively specific emergency and malfunction scenarios form the underlying basis, with the systems built to counteract and contain the predicted dangers. To give an example, supports for fuel rods in nuclear reactors are equipped with electromagnets, so that the rods will fall out automatically in the event of an electric power failure. Other examples include the so-called “safety strains” in genetic engineering which are expected to be unable to survive in the wild, and organisms bred with a “killer gene” which programmes them to self-destruct after a certain period of time.

There would seem, then, to be nothing wrong with pursuing the highly interesting and promising prospects for “inherently safe nanotechnology” or even “sustainable nanotechnology” while at the same time exploring the practicability of using guiding principles to develop and shape technology. The case should not, however, be overstated: it is clear that justifiable objections will be raised to the examples of inherent safety given above. It is axiomatic and self-evident that totally risk-free and inherently safe technology is impossible to achieve. But tangible progress on a gradual path towards inherently safe technology and/or towards inherently safe application systems - which include the human factor - should provide perfectly sufficient motivation and serve as an adequate measure of success.

Naturally, the question immediately arises as to whether - and to what extent - technological development influenced by guiding principles is capable of bringing about technology that is indeed more consistent with these ideals. The success of concerted intentional action within complex innovation systems should not be taken for granted. Unintentional results, i.e. the notorious side-effects and long-term effects which are the primary focus of technology assessment, can also of course be expected.

However, it certainly makes a difference whether or not the potentially detrimental impact on sustainability is taken into account in technological development and in the design of techniques and products. And this is, quite probably, equally true for possible beneficial effects. It should definitely make a tangible difference to the outcome if nanotechnology – as well as techniques and products derived from it – is specifically and selectively developed in terms of whether – and how far – it contributes towards the goal of risk minimization or the more far-reaching objective of sustainable development.

Provided all these assumptions are even approximately correct, then guiding principles such as “inherently safe” or even “sustainable nanotechnology” will not always result in developments that are worthy of these epithets, completely free of risks, detrimental side-effects and knock-on consequences. Nevertheless, it should be more likely that the actual outcome of development efforts will be more in line with the guiding principle. And this would be no mean achievement, given the never-ending difficulties and problems that we face in trying to subject (potential) technological outcomes (technologies, processes, products) to “retrospective” or even “prospective” technology assessment or sustainability assessment while completely neglecting the preceding development processes. In this context, we would like to endorse “guiding principle-oriented” action and devel-

opment as an (at least partial) solution to the fundamentally unsolvable dilemma of technology prediction and assessment. We will never know enough about the possible effects of technologies and other forms of intervention on societal and natural systems, and this is especially true when we are trying to predict the impact of a technology that has yet to be developed and introduced. A possible approach to “dealing with the unknown”, therefore, is to put attempts at prospective technology assessment on a level with efforts to ensure that technological development is governed by guiding principles. This means that the fundamentally insoluble problem of prediction in technology assessment is not only tackled by ever more sophisticated approaches to (and instruments for) prospective technology assessment<sup>10</sup>, but also by actively seeking to fulfil the predictions or, more accurately, achieve what is desirable. “Active implementation” may, after all, remain the most promising means of ensuring that prognostications actually become reality.

Technological development based on guiding principles may therefore provide an answer to the dilemmas associated with an approach to assessment that is fixated on *effects and consequences*. Knowledge about the possible impact of technologies (technology assessment) or substances (toxicology, ecotoxicology, industrial health and safety) will always essentially remain insufficient and incomplete. Both “worst-case scenarios” and “guiding principles” can offer guidance and suggest boundaries within which the process of exploration and innovation should operate, i.e. assist in averting what we categorically wish to prevent, and may bring us closer to our goal of inherently safe - or even sustainable - nanotechnology.

Elements of inherently safe nanotechnology might include the use of “inherently safe substances” within the boundaries of an “inherently safe technology” which in turn lies within the framework of “inherently safe application systems”. The uncontrolled dispersion of nanoparticles can probably be prevented by applying the following principles in shaping technology and choosing between alternatives: i) rapid loss of potentially harmful “nanoproperties” if emitted into the environment (e.g. through agglomeration), ii) rapid breakdown of used substances (biological and photochemical degradability), iii) low bioavailability and bioaccumulation of substances and particles, iv) restriction to “contained applications” (avoidance of open applications, very good containment).

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10 A second approach - the “characterization of a technology” - is proposed along these lines as a second attempt to circumvent the problems of prediction.

### 3 Guiding principles towards a “sustainable nanotechnology”

In choosing “sustainable nanotechnology” as a guiding principle, a technology-oriented approach was adopted. We took technology as the starting point, and enquired into its potential contribution to sustainable economic development and the associated opportunities and threats with regard to the goal of “sustainability”. We could, instead, have opted for one of two alternative or competing concepts: the “problem-oriented” or “need-oriented” approaches. The problem-oriented approach centres around climate protection, resource conservation or risk minimization; here, nanotechnology would form part of the picture only where it was expected to help solve the problem. The same is true for the need-oriented approach, for which guiding principles such as “sustainable building and habitation” would be the starting point. To reiterate: “sustainable nanotechnology” is, therefore, a technology-oriented guiding principle. Given that the development dynamics in nanotechnology are, in many sectors, still largely technology-driven, focusing on technology-oriented guiding principles appears to be a promising idea. Broadening the approach to respond to specific human needs should present no problem if the focus is on specific areas of use, i.e. sustainable “application” or sustainable “utilization” of nanotechnology, as for example in “ultra-light construction of (recyclable) vehicles on the basis of nanotube-reinforced materials”.

Successful guiding principles for sustainable nanotechnology should be vivid, pictorial and clear; they should motivate by communicating both value and purpose, and they need to be in touch with the true potential of nanotechnology (i.e. be grounded within the realms of the feasible; see above). It is certainly helpful to recognize varying timescales, with regard to both an agenda for achieving long-time goals and actual technical potential and feasibility. These could begin with the - possibly rapidly achievable - potential for “defensive” risk minimization or damage prevention, taking in medium-term development and planning horizons (such as technological “road maps” drafted by foresighted companies and branches of industry) and extending to long-term utopian blueprints for the future.

In the short-term perspective we might start by proposing, as a working concept, a guiding principle termed “**resource-efficient nanotechnology**”. For the medium term the principle of “**consistent and inherently safe nanotechnology**” would be adopted and, in the long term, “**nanobionics**”. These guiding principles should be mutually integrative in that the longer-term principles always incorporate the goals of the shorter-term ones. That is to say, nanobionics will also meet the demands of resource efficiency, consistency<sup>11</sup> and inherent safety.

These guiding principles are in part ‘extracted’ from the actual debate about the potentials of nanotechnology. On the other hand they are systematised constructions. They cannot (yet?) be fully articulated and presented within these pages. It is, in any case, rather improbable that any such proclamations from ivory towers (academic or otherwise) will be successful. If we are to test a guiding principle for its resonance, this will require debate - although such discourse should in no way be

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11 Consistency is taken here to mean the qualitative and quantitative embedding of the anthropogenic metabolism, or industrial metabolism, respectively, within the natural metabolism. This may occur through material and energy flows in the technosphere opening up to the ecosphere (e.g. through adoption of regenerative material and energy sources and through taking into account the biological or photochemical degradability of materials) or through a particularly effective sealing-off of the technosphere from the ecosphere (only “closed applications” and optimal containment).

restricted to collect already existing views, emotions and positions. Guiding principles must be far more than merely the lowest common denominator; they cannot simply be linked to the present collective awareness. Guiding principles need a generous helping of irritation and provocation – for it is these stimuli that often generate the best response.

In order to concretize these notions and as an initial contribution to public debate, some elements – admittedly, just the core aspects - of those guiding principles for sustainable nanotechnology are given below:

**Tab. 1: Guiding principles towards a (more) sustainable nanotechnology**

Source: von Gleich University of Bremen

Guiding principle	Theme/Maxim	Focus	Examples
Resource-efficient nanotechnology	As little harm and resource consumption as possible	The quantity of energy and material flows (life cycle-oriented) in relation to the benefits to society	Low-wear and low-abrasion surfaces (mechanical engineering) Highly specific membranes (biotechnology, fuel cells)
Consistent and inherently safe nanotechnology	Adapted to reflect the metabolic principles and capacities of nature as a whole and of human beings (minimal depth of intervention and high fault tolerance)	The quality and quantity of material and energy flows, and technical risks in respect to health and environment	Nanotubes Spiders' silk In lightweight structures biodegradable or recyclable
Nanobionics	"Learning from nature", life-supporting, cooperating with the principles of self-organization within our own bodies and nature as a whole <sup>12</sup>	The quality of technology (the form of interaction with nature)	(Bio)Catalytic converters / enzyme technology Bio mimetic materials synthesis <sup>13</sup>

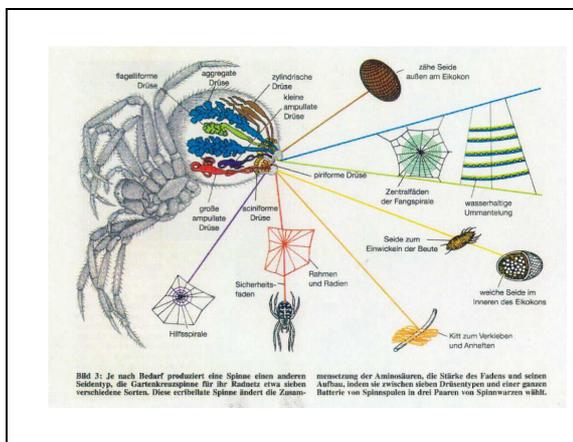
In order to "flesh out" these guiding principles, these remarks will be concluded by two examples – those of spider's silk and biomimetic materials synthesis – in order to demonstrate their nanotechnological potential, i.e. relate them to the often mentioned notion of feasibility.

12 A possible second-order guiding principle: co-productivity with nature in an "engineered alliance" (see Bloch 1973)

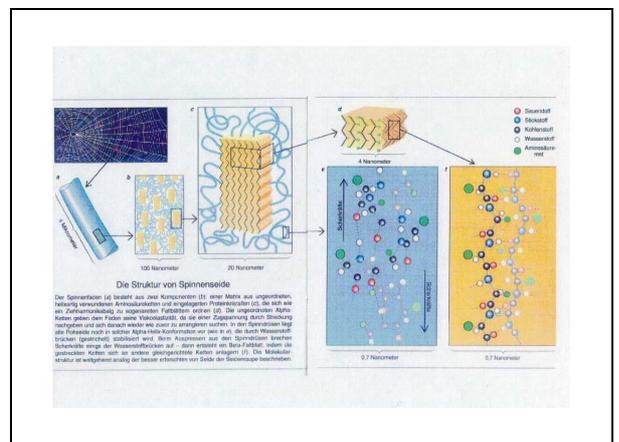
13 vgl. Niesen, T.; Aldinger, F. in: Arnim von Gleich (Hrsg.): Bionik – Ökologische Technik nach dem Vorbild der Natur? Stuttgart 2002

## Spiders' silk

In their diversity and combination of properties, the threads produced by spiders are a quite extraordinary building material. Certain spiders, having as many as seven spinnerets or spinning glands, are capable of producing threads with a multitude of different properties: for catching prey (elasticity, stickiness), for securely wrapping prey, for their own protection (durability), as an aid to mobility, and so on (Figure 1). A look at the molecular structure illustrates very nicely how spiders manage, “nanotechnologically”, to absorb relatively massive forces within their webs (Figure 2). The highly efficient use of a limited reservoir of materials is another fascinating aspect. In order to “dispose of” no longer needed threads, these fibres – which offer high-protein nourishment – are consumed by the spider. The silk of certain spiders is twice as tear-resistant as steel and up to 50 times as elastic as nylon. For some time now, spider's silk has been the subject of intensive re-



**Fig. 1: Silk production by spiders**  
Source: Vollrath (1992)



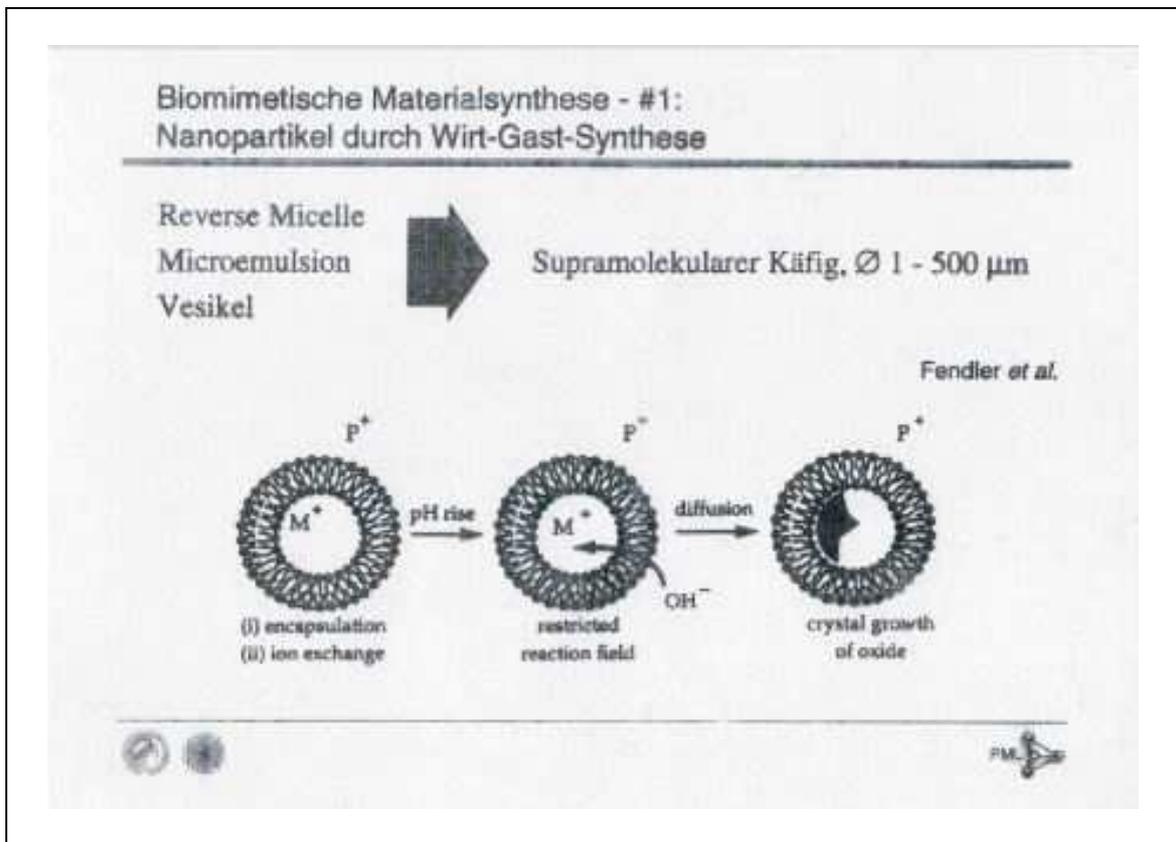
**Fig. 2: The structure of spider silk**  
Source: Vollrath (1992)

search in a number of centres worldwide; studies have, for example, been commissioned by the US Army in the hope that they may yield improved body armour and parachutes. Three different strategies for extracting spiders' silk are being pursued concurrently. One currently-used approach entails test spiders being “milked”, with up to 100 m of spider's silk extracted per day. This involves the animals being anaesthetized with CO<sub>2</sub> and immobilized. This solution may raise some ethical problems (with regard to the spiders), yet in terms of possible wider ecological repercussions it is relatively manageable, as it can best be compared to the traditional extraction of wool from sheep and silk from silkworms. The other two strategies involve synthesizing the silk by chemical means and implanting a gene coded for spider's silk into cultivable bacteria. Both methods have already yielded small quantities of spider's silk.

This example shows very effectively how “bionic” ideas drawn from nature can give rise to very different technological strategies (by no means all of which can be evaluated positively). Learning from nature, the starting point for bionic technology, therefore far from guarantees “inherently safe and environment-friendly technology”.

## Biomimetic materials synthesis

Achieving the ability to self-organize was a crucial step in the evolutionary transition from inanimate nature to animate forms (see, for example, Eigen's works on the "Hypercycle" [Eigen; Winkler 1978] as well as Maturana and Varela's work on autopoiesis [Maturana; Varela 1987]). Rudimentary forms of self-organization can, however, also be found in the non-living natural world. The alignment of molecules according to their electrical charge is one example. "Polar molecules", which have a hydrophilic and a hydrophobic pole and are key constituents of cell membranes, are a further well-known example. If a water surface is coated with a thin, preferably single layer of these molecules, they automatically align themselves into a "self-assembled monolayer". Figure 3 shows the outcome of a three-dimensional self-organization process.



**Fig. 3: Principle of the segregation of a ceramic layer from a solution of functionalized self-assembled monolayers (SAMs)**

Source: Aldinger (1998)

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# Potential ecological and health effects of nanotechnology;

## Approaches to prospective technology assessment and design

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Overview:

1. Procedures, methods and criteria within technology assessment
2. The problem of prediction
3. Managing the unknown
4. The “characterization of technologies” approach
5. Technology-specific effects: “Size does matter!”
6. Trial and error as the most widespread form of technology assessment; its limitations
7. Consideration of application contexts
8. Conclusions

### **Introduction**

If technologies are to be designed and developed with a view towards both safety and sustainability, it is essential to carry out technology assessment at an early stage and to understand the different types of innovation process involved.

The aim of this contribution is to help answer the following questions, which are important in the assessment, promotion and shaping of nanotechnology:

What can we know? And what can we do?

- a) What methodology should we follow? How can the prospective assessment of an emerging technology be more than blind, haphazard guesswork?
- b) Is there a technology-specific reason for explicitly focusing on nanotechnology? Why is so much attention directed to the potential beneficial and/or detrimental effects of this form of technology? Just how potent and/or versatile is it, and does it qualify as a “power technology” and/or “key technology”?
- c) Which aspects require specially careful consideration in the development and design of this line of technology? In particular, what role can guiding principles play in helping us adopt a precautionary approach in steering the course of nanotechnology?

# 1 Procedures, methods and criteria within technology assessment

It is not the aim of this project to facilitate comprehensive sustainability assessment. The focus is on ecological and health effects, i.e. both on the intended opportunities and the unintended risks and side-effects; both on more easily identifiable short-term effects and less easily anticipated long-term consequences.

Scientifically endorsed technology assessment is based on reasonably well-established and formalized assessment procedures, methods and criteria.

The procedures include not only political discussion forums involving the public, consensus conferences, hearings and e. g. Enquete Commissions set up by the German parliament, but also environmental impact assessments, approval procedures and legal proceedings. The key methods employed include risk assessment, ecotoxicological and toxicological testing, cost-benefit analysis and life-cycle analysis. Examples of assessment criteria are resource consumption, greenhouse potential, impact on habitats and biodiversity, water pollution class, and acute and chronic toxicity. Ultimately, the assessment methods used should - in conjunction with assessment criteria - provide rigorous (i.e. for the most part scientifically sound) arguments for economical, political and public debates about choices of technologies, processes and products.

## 2 The problem of prediction

In attempting to gauge impact, all forms of technology assessment come up against the problem of prediction. Our knowledge of the potential effects of substances, techniques and application systems is limited by:

### i) the as-yet-unknown

This is knowledge that is basically attainable but not yet available, perhaps because certain tests have not yet been carried out or because experience is still lacking in particular areas. There may be many reasons for this, such as total unawareness of the potential problem (as with the ozone-depleting effects of CFCs) or lack of resources (e.g. time, money, and manpower). A typical example is the specific effects for which chemical substances not registered before 1982 have yet to be tested (e.g. acute toxicity, CMR, biodegradability, bioaccumulation, etc.).

### ii) the unknowable

For fundamental reasons, the ways in which unstable, complex and dynamic systems respond to intervention cannot be predicted. The reasons for this “unknowability” lie primarily in the system’s intrinsic “architecture”, that is to say the unstable condition of the systems within which the intervention takes place. However, the “intensity” of the intervention, in terms of both quality and quantity, also plays an important role.

Examples include the unforeseeable response of ecosystems to the existence of “gaps” in their food chains or the unpredictability of the isolated, spatially and temporally limited effects of climate changes (e.g. when and how will the Gulf Stream react?).

### 3 Managing the unknown

Certainty is the exception! Uncertainty is the rule! When predicting the impact of an emerging technology, the inescapable problem of prediction becomes acute. In view of this situation, shifting the onus of proof back and forth is a well-loved but utterly fruitless game. Neither the potential hazard-ousness nor innocuousness of a technology can be “proven”. And neither the “novelty” of a technology, nor lack of knowledge about its potentially problematic consequences, constitutes good and sufficient grounds for “great concern” or even for a comprehensive “moratorium”. Newness and insufficient experience justify “circumspect behaviour” - which is true for any non-routine activity in everyday life.

In order to warrant such “great concern”, and in turn taking comprehensive measures in accordance with the “precautionary principle”, further reasons are required. These reasons are generally intrinsic to the technology itself (e.g. extremely high potential impact, considerable depth of intervention) or the specific application contexts (intervention within an especially vulnerable, unstable and important system).

“No innovation is without risk!” is a fundamental truth. But what counts is the level of potential risk, and this is usually determined by:

- i) the **quality of the intervention** (identification of high-risk technologies);
- ii) the **quantity of the intervention** (identification of cumulative effects); and
- iii) the **quality of the system** subjected to the intervention.

The development of sensible (rational and value-oriented) ways of managing uncertainty, and especially ‘dealing with the unknown’, is among the core tasks of “reflexive modernization”.

Important prerequisites are:

- i) analysis and characterization of the technology (i.e. of the type of intervention); and
- ii) analysis and characterization of the systems subjected to the intervention. Here, the systems directly affected are the technical application systems, with human health and/or ecosystems affected indirectly.

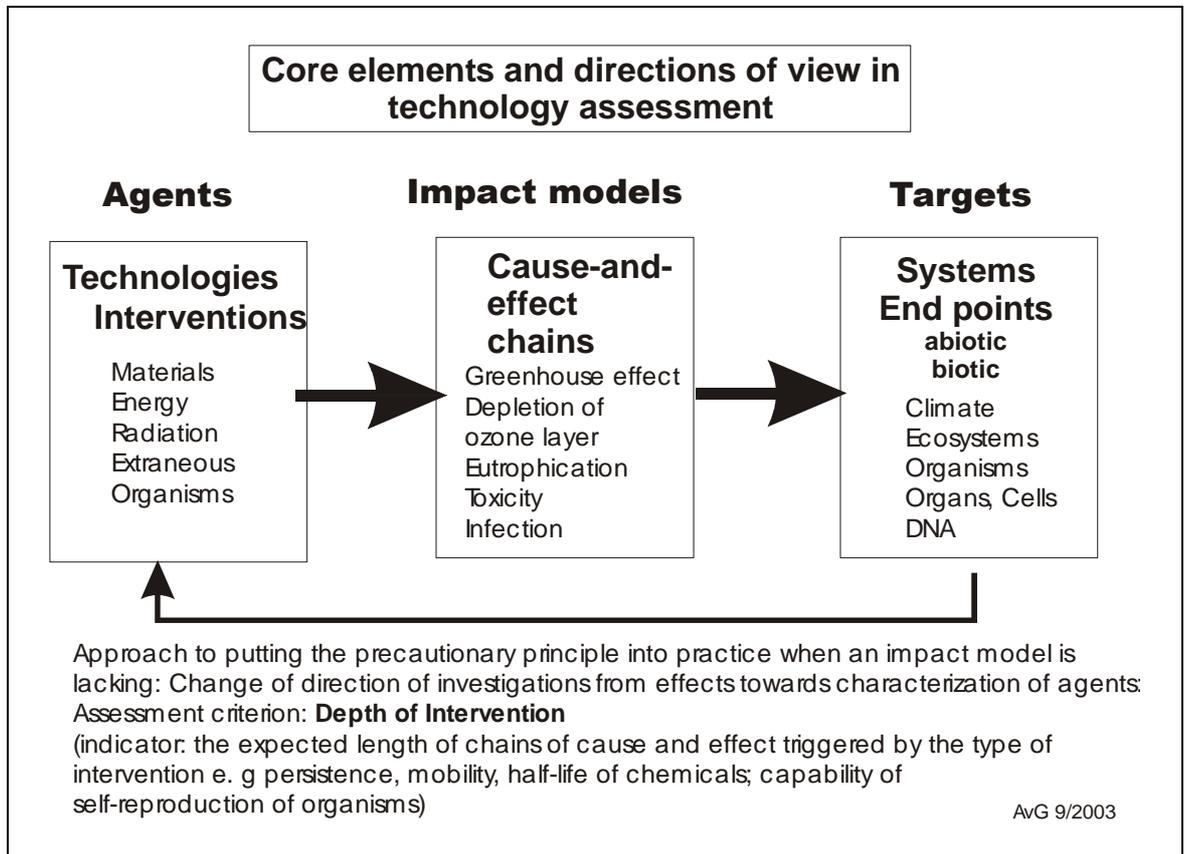
### 4 The “characterization of technologies” approach

In response to the opinion - still frequently voiced - that technology itself is neutral, and only its various applications can be subjected to value judgements, we can say that technology is always a “way of dealing” or “form of interaction” with something. It cannot, in consequence, be neutral. At the same time, however, the question “to what use is it put?” is important in terms of its assessment.

Knowledge about impact (the central prerequisite of technology assessment) requires familiarity with three basic elements:

- i) An agent (the technology, substance etc. whose possible effects are to be assessed);

- ii) An impact model (i.e. a scientifically verifiable theory on how the agent acts on a potential target. Examples include: the greenhouse effect; skin cancer resulting from stratospheric ozone depletion; and effects that are carcinogenic, mutagenic or toxic to reproduction (CMR); and
- iii) A target upon which the agent acts (e.g. climate, ecosystem, organism, or organ).



**Fig. 4: Core elements of technology assessment**  
 Source: von Gleich, University of Bremen

It may be that all three elements are unknown quantities. In our technology-oriented case, it is the impact model and/or the target system that are the unknowns. The proposed approach to problem-solving in technology assessment is to change the focus by changing the view from the potential target systems towards a closer look at the agent which is going to act upon them. The emphasis is, therefore, on the characterization of the “agent”, in our case nanotechnology. We have to address the question of what (potential) effects can be expected or deduced simply by virtue of the “nano-scale” of the interventions.

## 5 Technology-specific effects: “Size does matter!”

Let us now take a look at what makes nanotechnology so interesting:

i) Its **potency** and **depth of intervention** (the possibility of controlling the smallest building blocks of matter or – conceivably - of living things). To what extent is nanotechnology a “power technology” and/or a “high-risk technology”?

ii) The “**new effects**” achievable through its use. Where does nanotechnology merely improve and enhance existing possibilities and effects - and where does it bring about qualities that are truly new and unprecedented?

iii) Its **versatility** in both possible effects and applications. To what extent is nanotechnology a key technology and/or a fundamental innovation?

The following list gives some immediately obvious nano-specific aspects and effects, together with some of the possible (or expected) properties and effects based thereon.

### **Nano-specific aspects/effects**

1. Small size

=> Mobility

=> Perceptibility/detectability

2. Specific surface area-volume ratio

=> Adhesion, cohesion, agglomeration

=> Altered chemical reactivity and selectivity

=> Catalytic effects

=> Quantum effects

3. Self-organization

=> Uncontrollable, autonomous developments, replication

Also to be mentioned:

4. Precision of the specification and substance quality<sup>14</sup>

=> Chemical purity

=> Defined particle size

=> “Rare”, and perhaps problematic, elements and groups of substances

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<sup>14</sup> These properties are not unique to nanotechnology, nor do they hold true for all of its applications. However, if a characteristically high level of input is unavoidable in the production of nanomaterials, nano-scale process materials and nano-scale auxiliary substances, then this will be highly relevant in terms of impact, at least with regard to life-cycle analyses.

## Potentially problematic “nano-specific” effects

Here, too, the question of “required input” and “quality of substances used” are to be dealt with first, although the related issues are not always solely restricted to nanotechnology.

### 0.1 Precision of the specification of materials; demands on production

Quality and quantity of substance and energy flows in the production of nanomaterials and particles.

Strict requirements may exist with regard to precision of specification of input materials (especially degree of purity and particle size).

Highly demanding production processes are only justified if the effort “pays back” during the product life cycle

Questions of recyclability and the time and effort involved in recycling (entropy balance).

### 0.2 Substance quality

Are the elements or groups of substances used either rare or known to be problematic?

- e.g. use of gallium arsenide in semiconductors, heavy metals as catalytic converters
- Ratio between “natural” and “anthropogenic” conversion of substances as an indicator in ecosystems?

The following headings relate, respectively, to points 1 – 4 above.

#### 1) Small size => particle mobility

- Are the particles dust-like in behaviour, i.e. “mobile” in air, not settling but remaining suspended in the air?
- Are they able to reach the lungs or even the alveoli (detrimental impact strongly size-dependent, perhaps even completely unrelated to substance quality)?
- Can they pass through the cell membranes (and cross the blood-brain barrier, or come into contact with DNA)?
- Is there a potentially mobilizing or “piggyback” effect on problematic substances or groups of substances: toxins, heavy metals?

#### 2) Adhesion, cohesion, agglomeration

- Adhesion, cohesion and agglomeration effects render technical handling more difficult but, since they may also effectively “cancel out” the nano-properties, this may on the other hand contribute towards “inherent safety”.

Behaviour of “released” particles or fibres in the “environment”?

#### 3) Altered chemical reactivity and selectivity, catalytic effects

- Some toxicological and ecotoxicological “surprises” are highly likely, as are sensitizing effects
- Photocatalytic effects?

#### 4) Quantum effects

It is unlikely that quantum-related side-effects will be detrimental to organisms and ecosystems, because many of the “quantum effects” relevant within nanotechnology only occur in extremely pure and very well-defined “technical environments”.

Conversely, “contamination” and “disturbances” within well-defined systems are likely to be a significant source of “faults” and “malfunctions” which may have rather far-reaching implications (this raises the question of inherent safety and fault tolerance within an application system).

## Self-organization and uncontrollable developments

From various standpoints, including that of sustainability (at least on the level of materials and energy input), among the most promising technologies are those that exploit molecules' ability to align themselves responsively, move and combine – i.e. their ability to self-organize. These self-organization effects, together with the use of the sun as an energy source, constitute the basic principles of evolution and ontogenesis. Technologies that are based on deliberate cooperation with natural processes of self-organization may be termed nanobionics (also serving as a potential guiding principle).

However, when this is taken further, making it possible to actually influence or **control** at the molecular level, then we are in the realms of the most potent technologies, although these often require specific “environmental conditions”.

Self-organization must be distinguished from self-reproduction, as shown for example by genetically modified organisms.

It is rather unlikely that nanotechnology alone will make the “quantum” leap towards self-reproduction and multiplication. It remains to be seen whether this step can be achieved by combining nanotechnology with genetic engineering.

We therefore need to consider more closely the following question: how soon will nanotechnology reach the point in its progression where we can expect it to manifest the ability to self-reproduce and multiply; at which developmental stage might it become an autonomous, uncontrollable, high-risk technology? The currently foreseeable exploitation of self-organization principles in nanotechnology (nanobionics) does not rely on profoundly influencing the vital control mechanisms (such as those regulating cerebral, hormonal and genetic systems). Rather, it depends on decentralized contextual control (substance gradients), or involves utilizing commonly found chemo-physical properties of molecules in a controlled environment. As long as this holds true, uncontrollable developments (self-reproduction and self-multiplication) are rather unlikely to occur.

**Tab. 2: Nanoqualities and derived problematic ,nanospecific' effects**

Nanoquality	Effect/problem	Approach of assessment	Non-nano examples
<b>Well defined particle size and purity</b>	Material and energy streams, resource consumption recycling	Life-cycle-analysis, entropy balance, ,ecological amortisation?'	Technical ceramics
<b>Material quality</b>	Health and environmental hazards, problematic (rare) elements or groups of materials in open use	Toxicology, Ecotoxicology, Ratio between ,natural' und ,anthropogenic' material streams	Gallium-arsenide in semiconductors Heavy metals in catalysts
<b>Smallness and mobility of particles</b>	Dusting, mobile in the air, remaining suspended entering the lungs and even the alveoli passing through cell membranes, the blood-brain barrier	Models of dissemination and exposition (Eco)toxicological (animal) tests, epidemiology	CFCs (mobility and persistence) Ultra fine particles from diesel engines
<b>Adhesion, cohesion, agglomeration</b>	Fate of emitted nanoparticles or fibres in environment, ,intrinsic safety' by tendencies towards adhesion, cohesion and agglomeration?	Models of dissemination and exposition (Eco)toxicological (animal) tests, epidemiology	Metal-ions in soil with mobilising and piggyback effects

Nanoquality	Effect/problem	Approach of assessment	Non-nano examples
<b>Changing chemical reactivity and selectivity</b>	Altered ratio between surface and content leads to massive changes in catalytic reactivity, unexpected toxic and ecotoxic effects are highly presumable,	Toxicology, including sensibilisation	Problematic effects of ultra fine particles seem to be strongly dependent on size far less on quality of substance <sup>15</sup>
<b>Changing and intensified catalytic effects</b>	Altered ratio between surface and content leads to massive changes in catalytic reactivity, unexpected toxic and ecotoxic effects are highly presumable, also photocatalytic effects in inorganic (atmosphere) and organic areas	Models of dissemination and exposition (Eco)toxicological (animal) tests, epidemiology Toxicology, including sensibilisation	
<b>Quantum effects</b>	Mostly depending on highly defined and purified conditions, where impurities are a source of technical failure. In the environment side effects in organisms or ecosystems are more or less unlikely	Risk analysis For technical systems: FMEA	
<b>Self-organisation</b>	On one hand highly promising for resource efficient technology, consistent with natural processes, on the other hand hazard of uncontrollable developments (self-eplicating nanobots)	Technology assessment risk analysis, scenarios	Self Assembled Monolayers, Bio mimetic materials,

## 6 Trial and error as the most common form of technology assessment; its limitations

Trial and error remains the basic principle on which technology assessment is based. This is inevitable for pragmatic reasons (resources of assessment, time, money and manpower), fundamental reasons (unknowability) and societal reasons (intensification of international competition with regard to innovation). For many - and probably most - of the stages involved in innovation, this does not present too much of a problem. "Trial and error" is, in theory at least, a fully adequate approach when small and (in principal) reversible steps are involved within fairly robust systems. However, even the principle of trial and error need not - and should not - be used "blindly and randomly" in technology assessment, but "consciously and methodically". One of the most important prerequisites for such use is the accurate and specific monitoring of "trials" based on relatively comprehensive knowledge; this is especially critical during this "test period" when the new technology is on trial. To this end, when developing and introducing nanotechnology the focus should be on:

15 For epidemiological results see Dockery; Pope 1994 and Pope; Dockery 1999., for experimental results Diabaté; Völkel; Wottrich 2002

- i) nanospecific effects; and
- ii) certain consciously selected application contexts.

The usefulness of the trial-and-error approach is, however, limited with regard to innovative developments, i.e. when employing highly potent and “deep-acting” technologies with very far-reaching expectable consequences (chains of cause and effect in time and space).

The principle of trial and error can no longer be applied where – based on information about the nature or quality of the technology used, the intervention itself or the system affected – it appears that a given intervention would entail undertaking a large-scale, irreversible experiment that may jeopardize entire areas or ecosystems, or the livelihoods of future generations. In other words, the limit is reached at the point, if not before, where a tendency towards global and irreversible effects is expectable, intensified all the more by high-input use with cumulative effects.

A classic example of where the limitations to the trial-and-error approach went unheeded is seen in the release of CFCs – with global and irreversible consequences - despite prior knowledge of at least some very problematic properties shown by this group of substances:

- i) little known (rare, unnatural) substance quality
- ii) persistence
- iii) high mobility;

In combination, these three properties alone led to CFCs appearing virtually all over the world, including locations where environmental conditions may have been unknown or where the relevance of these conditions was not fully realized (e. g. the stratosphere).

Situations in which the approach of trial and error is unsuitable include those where the intervention runs very deep (e.g. interference with control principles and/or fundamental system processes) or where it involves the ability of self-replication, as in the release of genetically modified organisms.

## 7 Consideration of application contexts

It is essential that the various approaches to the “characterization of technologies”, as presented above, are subjected to critical debate in terms of their justification and reasonableness, and especially with regard to their practical feasibility and scope. The “characterization of a technology” would appear to be a fairly manageable task in this respect. It is far more difficult to appraise application contexts and to analyse and characterize the affected systems in respect of their “architecture” and stability. In terms of quality and quantity, the impact of a technology is the product not only of its intrinsic nature, but also of the specific context in which it is applied.

To name but a few well-known examples of these effects: technologies can intensify or weaken trends within society. Technologies can be misused. Even when the underlying technologies are generally harmless (inherently safe), intervention within particularly vulnerable systems may have an impact that is both global and irreversible (e.g. the effect of Thalidomide on embryonic development); the risk is accentuated still further when, even in comparatively stable systems, quantitative cumulative effects come into play (as in the anthropogenic greenhouse effect).

A prospective assessment of the potential impact of nanotechnology on ecosystems and health cannot focus solely on the characterization of the technology and on nanospecific effects. It must also consider trends within society and the peculiarities of specific application contexts.

## 8 Conclusion

Taking into account our present-day knowledge there is, with regard to foreseeable nano-specific effects (including self-organization effects), no reason for “particularly great concern” on a par with the justifiable apprehension concerning nuclear technology and genetic engineering.

The nature and level of risk that can be anticipated, based on currently available data, is perhaps most akin to that associated with (synthetic) chemistry. From a historical perspective, however, the risks of the latter have proven “quite considerable”.

If we are to avoid making the numerous mistakes seen in the field of chemistry, then it is necessary to assess and consciously shape technologies – and to adopt precautionary measures - at an early stage. The REACH system outlined in the current EU White Paper on Chemicals Policy prescribes risk analysis and management procedures which are probably also adequate for most nanotechnological applications. With regard to risk management, too, much can be learned from the chemical industry and from the handling of chemicals. However, the risk management of chemicals still has shortcomings with regard to implementing the precautionary principle (“inherently safe substances, techniques and application systems”). This includes the still widespread failure to incorporate available precautionary measures in the development of substances and technologies, and therefore the neglect of guiding principles as “instruments” of influence and design.

Thus a double-track approach may be the most promising concept for the “sustainable nanotechnology” project:

a) Identify the technology-specific impact mechanisms of nanotechnology. It is especially important to establish more firmly the appropriateness of, and soundness of reasoning behind, the “characterization of technologies” approach and to improve its (differentiating) power to predict possible effects.

b) Choose and justify particularly “interesting” application contexts, which may include:

i) those with a particularly high degree of intrinsic sensitivity (in terms of the quality and architecture of the affected systems). Here, risk assessment would be the method of choice.

ii) those which exhibit a considerable social dynamic in any case (because of potential intensification, mass and cumulative effects, and level of input). The preferred instrument here is life-cycle analysis.

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# The environmental impact of nanotechnological processes and products

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Assessment of the environmental impact of nanotechnologies has, to date, been viewed primarily in terms of opportunities (“radical green vision”), with risks seen mainly in connection with the possible long-term trend towards the development of “self-replicating nanorobots”. Exposure to these risks is to be reduced through so-called “foresight guidelines”, which chiefly address how to shape technologies in order to ensure that they do not get out of hand.

It is only more recently, partly in connection with the transition to industrial production (especially of nanoparticles) that reservations have been voiced with regard to certain aspects arising from the intrinsic nature of this technology.

In this paper I will:

1. address the issue of nanotechnologies;
2. address the issue of time frames;
3. refer to results from recent studies, placed in the context of the characterization of the technologies; and, finally,
4. outline the specific needs for R&D in nanotechnology, derived in part from the so-called road maps for the chemical industry.

## 1 The issue of nanotechnologies

The term “nanotechnology” tends to be used rather loosely. In its broadest sense it includes all those technologies and processes which operate on the nanometric scale. This implies that it embraces a wide variety of sectors and, therefore, that we can expect to see all manner of different technologies becoming integrated under the banner of “nanotechnology”.

The handling of nanomaterials is not a fundamentally new phenomenon; nanoparticles, for example, have long been used in tyre manufacture. What is new, however, are the basic “aspirations” of nanotechnology: the technology is now seen in terms of controlling and shaping molecular architecture - forming, as it were, a transition between the “non-aware” dealing with nano-scale materials and the conscious attempt to manipulate these materials.

The basic idea that we can exert control over molecular architecture goes hand in hand with the notion of altered concepts of production, i.e. the change from conventional “top-down” approaches to “bottom-up” methods. This paradigm shift in production could also, in principle - leaving aside the undeniably huge technical difficulties that would be faced – lead to substantial improvements in the efficiency of resource use (with, for example, large reductions in waste production).

It must be emphatically stated, however, that both production paradigms will exist side by side in the longer term. To illustrate this using the above-mentioned example of tyre manufacture: the creation of nanoparticles serves to enhance the properties of tyres, but without there being any sweeping changes in the production process itself.

## 2 Time frames

Notions of how nanotechnologies might develop have sparked a great deal of controversy, although it should be noted that concerns being aired relate mainly to possible long-term trends (e.g. towards self-replicating nanorobots).

For example, Rocco (2002: 5) gives the following time frames (in terms of “generations”) for industrial prototypes and marketing in the field of nanotechnology:

- Nanotechnology has - in the form of carbon black, for example - been used “inadvertently” for centuries
- There have been isolated applications (catalytic converters, composites, etc) since the 1950s and, after more became known about nanostructures, since the beginning of the 1990s
- First generation: passive nanostructures (around 2001)  
Fields of application: coatings, nanoparticles, bulk materials (nanostructured metals, polymers, ceramics and ink-jet products)
- Second generation: active nanostructures (around 2005)  
Transistors, amplifiers, adaptive structures, etc.
- Third generation: 3D nanosystems (around 2010)  
With heterogenous nanocomponents and different assembling techniques
- Fourth generation: molecular nanosystems (around 2020)  
With heterogenous molecules, based on biomimetics and new design

The distinction, introduced above, between the technology itself and the various contexts in which it can be applied means that a host of different questions, involving different timescales, arise with regard to ecological sustainability assessment.

One requirement is for assessment directed at the “first generation“, involving life-cycle analysis and (eco-)toxicological assessment. Attempts must also be made to attempt to predict the possible consequences arising from the subsequent generations, and the fourth generation in particular.

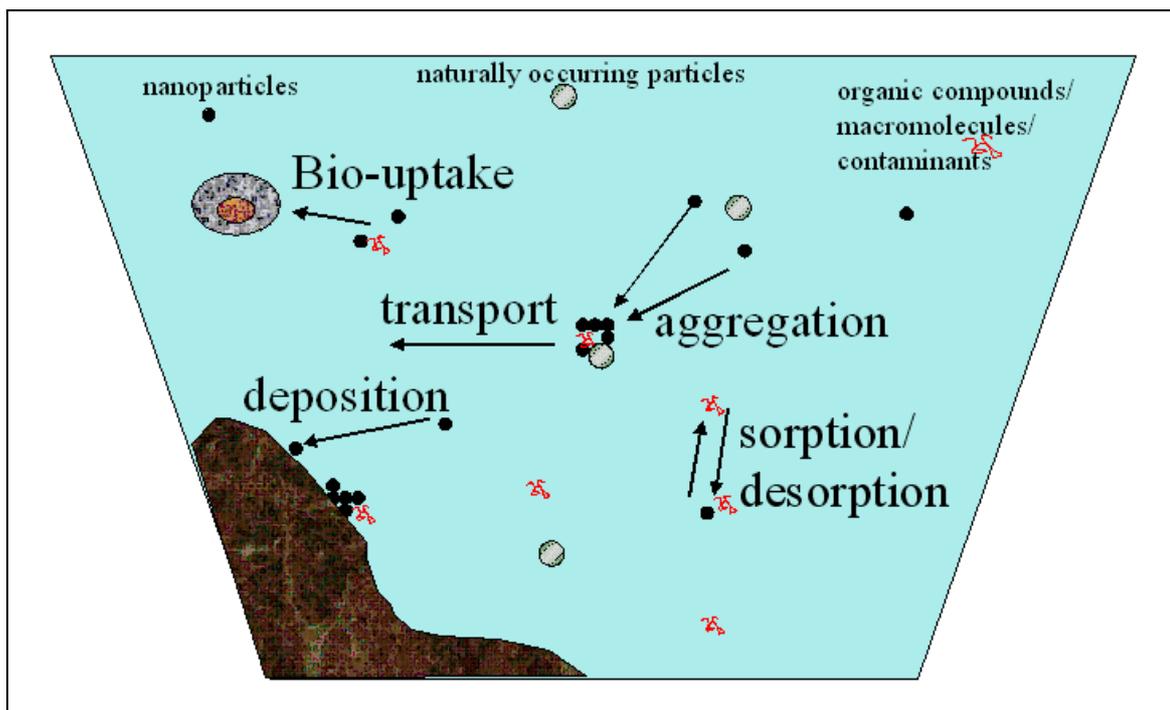
The main focus must be on the ecological sustainability of these conceived paths of development, and on the unintended side-effects.

Further expected advances in nanotechnology, however, will entail characteristic risks similar to those which play a part in genetic engineering. These risks are typified by those inherent in the so-called “wet nanotechnologies“ which are involved mainly with cells (termed “nanomachines“ in the jargon of nanotechnology). This also applies to the so-called self-replicating nanorobots – the feasibility of which has been called into question – and are, in terms of the problems generated, the inorganic equivalent of genetic engineering.

At the same time, it becomes clear from these conceptual phases that both risk management and the assessment of opportunities and threats are approaches that need to be applied at different levels. In the following, I will primarily address those environmental and health-related aspects of nanotechnologies that we already face today, and not the long-term developmental tendencies in this field.

### 3 Behaviour of nanoparticles and their potential impact on the environment and health

Based on the typification of the technology (i.e. nano-specific aspects/effects; see above), different



Source: Colvin 2002

potential effects may be seen. The following diagram illustrates how nanoparticles may behave, and their possibly unintended knock-on effects.

The above figure indicates the probable behaviour of nanoparticles in the environment and focuses mainly on bioavailability (bio-uptake), means of aggregation and transport, sorption and desorption, and finally deposition. It is important to note that it is a schematic generalization; differentiation is required when looking at real, specific situations, depending on which substances or combinations of substances are involved.

From the characteristic nano-specific aspects and effects described above, it is clear that the key attributes are small size and, in particular, the specific ratio between surface area and volume. These properties give rise to problems of adhesion, cohesion and agglomeration, as well as altered chemical reactivity and selectivity. However, this provides no conclusive information about the possible impact on the environment and health. With regard to the potential nano-specific effects on safety, health and the environment, little scientifically verified knowledge is currently available; instead of hard facts, what we have is a great deal of informed speculation and many warnings. Some of this evidence is given below. Nanoparticles, which are already produced and used on a large scale, do not however constitute a fundamentally new problem. It is - not least owing to increasingly sophisticated measurement techniques – largely concern over emissions from diesel vehicles that has made these nano-scale particles the subject of debate.

## Nano-specific aspects

Given below are a number of brief quotations from the literature on the behaviour of nanoparticles and nanomaterials. It must be stressed that these do not allow any confident predictions to be made as to the actual hazards involved. Nevertheless, these extracts do indicate certain potential risks.

### *Prevention of air pollution*

With regard to technical measures aimed at air pollution abatement – and hence a generally problematic situation – one study reached the following conclusion: “It emerged, however, that technical improvements led to an efficient reduction only in the coarser dust component (> PM 10). Whereas there was a substantial reduction in those particles that only reach the upper bronchii, those taken up by the lungs (respirable particles: PM 2.5 and PM 0.1) showed a far less marked decline. The concentration of ultrafine particles (PM 0.1) in respiratory air actually increased” (Eikmann; Seitz 2002:63).

These remarks pertain only to nanoparticles found in vehicle emissions, not those discharged in nanoparticle production or those released through the use of certain products. Nevertheless, there is growing unease about these particle emissions, given the possible health risks.

### *Water*

Mark Wiesner of the Center for Biological and Environmental Nanotechnology (CBEN) is researching the behaviour of nanomaterials in water and has reached the following conclusions: “nanomaterials can move with great speeds through aquifers and soil [...] nanomaterials provide a large and active surface for sorbing smaller contaminants, such as cadmium and organics. Thus, like naturally occurring colloids, they could provide an avenue for rapid and long-range transport of waste in underground water.”

An international research project found that effluent from mines contains very high concentrations of dissolved heavy metals and aluminium. Nanoparticles can spread these heavy metals to streams and rivers (see Vista Verde 2002).

### *Behaviour in the organism*

“Based on studies of naturally occurring nanoscale particles such as ultrafine particle aerosols and surgical wear debris from implants, we can speculate that nanoscale inorganic matter is not generally biologically inert. However, without hard data that specifically addresses the issues of synthetic nanomaterials, it is impossible to know what physiological effects will occur, and more critically, what exposure levels to recommend” (Krane 2002).

### *New materials*

A number of publications draw comparisons between nanotubes and asbestos; however, no relevant study-based findings have yet been published (see Small Times 2002).

Although the industrial production of nanotubes appears to be fairly imminent, few toxicological experiments have been conducted. Researchers have yet to investigate what happens when people inhale these nanotubes or when they enter the body during medical treatment<sup>16</sup>.

The extent to which these materials are biodegradable is also unclear. For example, fullerenes are assumed to be biodegradable, whereas nanotubes are thought not to be.

## **Risk assessment case study: legal proceedings at the Administrative Court of Baden-Württemberg**

In an initial judicial review of the approval of a plant for producing nanoparticles, a number of critical aspects were assessed by means of statements made by expert witnesses. All the specialists who were called in noted that the effects of nanoparticles on health have, as yet, been far from adequately researched. Overall, however, the expert witnesses consulted in these proceedings noted that the discussion process with regard to new assessment criteria is still ongoing. By analogy with the assessment levels of diesel soot and the additional emission load from the production facility, the expert witnesses' evaluation was that the conditions for approval had been sufficiently met.

Two aspects of this lawsuit are briefly outlined below.

- Permeability of cell walls to nanoparticles  
There have been isolated studies which conclude that “in animal experiments, after particles are introduced into the airways, these are subsequently detectable in substantial numbers in the liver, and must therefore have been carried there in the bloodstream. These findings should, however, in his estimation (i.e. that of Professor Wichmann, called in as an expert witness), be viewed with caution” (Verwaltungsgerichtshof Baden-Württemberg 2002:28).
  
- A completely new kind of potential hazard  
“The plaintiff asserts that the nanoparticles emitted from the witness' plant, which are produced specifically for commercial purposes, represent a completely new form of potential hazard which cannot be compared with that from ubiquitously present nanoparticles. However, the expert witness was not able – despite certain reservations - to confirm the existence of a new kind of potential hazard” (Verwaltungsgerichtshof Baden-Württemberg 2002:35).

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16 The reader is referred, however, to the few studies which dismiss the problem as of no great relevance (see Freitas 2002; Huczko et al. 2001).

*Aspects relating to life-cycle analysis*

As yet, no life-cycle analyses for nanotechnological processes and products have been conducted. The IOEW has begun to develop eco-profiles, which show that the potential for relieving the burden on the environment could be very great. For example, marked beneficial effects were identified in relation to the catalytic converter in automobiles. These findings need to be qualified, however, as there are a number of gaps in the data, relating to both how input-intensive the nanoparticle production process is (in terms of energy consumption and the chemicals used) and the impact of the possible release of nanoparticles into the environment.

## 4 Need for research by the chemical industry – as seen by industry, regulatory authorities and researchers

In 2002 a workshop entitled “Nanomaterials and the Chemical Industry – R&D Roadmap Workshop”<sup>17</sup> was held. Its chief aim was to identify the technical objectives and difficulties in the application and marketability of nanomaterials within the chemical industry and the key requirements for R&D derived therefrom. Further aspects - pertaining to safety, the environment and health – were also identified. It should be pointed out that discussions on these three areas were restricted solely to problems directly pertaining to them that could result from use of nanoparticles and nanomaterials. Longer-term problem areas were barely touched upon in this respect.

These other areas are referred to below, since these fundamental questions are of importance for further research efforts, in that they basically constitute a research agenda for nanotechnology.

There are many possible impediments to market development that result from a lack of knowledge about the safety, environmental and health impact of nanomaterials. They include:

- A lack of knowledge about the airborne dispersal of nanoparticles
- A lack of knowledge about environmental concentrations of nanoparticles (problem: measurement and quantification)
- Great uncertainty concerning the upscaling of production, as no environmental standards exist
- Insufficient knowledge about health risks of nanomaterials
- A lack of data on toxicity
- Insufficient experience with regard to the safe handling of nanoparticles
- Largely inadequate knowledge about the impact on health, safety and the environment

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17 Vision 2020 (2002): Nanomaterials and the Chemical Industry – R&D Roadmap Workshop. Preliminary Results. Workshop held on September 30; October 1 and 2, 2002. Chemical Industry: Vision 2020 - Technology Partnership.

This led to the following research priorities being drawn up:

- Development of models to enhance understanding of the inhalation and uptake of nanoparticles and their transfer to the blood circulation or tissue
- Investigation of the short- and long-term effects of health risks caused by nanoparticles
- Investigation of the breakdown of nanocomposites / the release of nanoparticles into the environment

*R&D requirements:*

- Studies on the toxicological properties of nanomaterials which are adsorbed by microparticles, and on the aggregation of nanomaterials
- Compilation of health, safety and environmental data on nanoparticles in various composites
- Toxicity testing and studies
- Interaction of nanoparticles with human physiology
- Life-cycle aspects of nanoparticles
- Modelling aimed at designing environmentally-friendly nanomaterials
- Development of rapid screening processes
- Methods and criteria for measuring the toxic effects of nanomaterials under conditions of use
- Recycling / immobilization
- Commissioning of environmental impact studies and life-cycle analyses (LCA)

*Main output of this high-priority R&D work*

- Comprehensive understanding of human toxicity as caused by nanomaterials
- Rapid results for new materials
- Adequate understanding of the environmental impact and the indirect effects on health

Overall, it can be noted that we currently have only minimal knowledge of the impact of nanotechnologies on safety, the environment and health, and that this - especially from the point of view of industry - may hinder the development and marketing of these technologies. It must be stressed, however, that the problems mentioned are not fundamentally new ones; the main problem issue surrounds the methods of assessment that need to be applied in, for example, the chemical industry.

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# Concept for assessing specific nanotechnology applications

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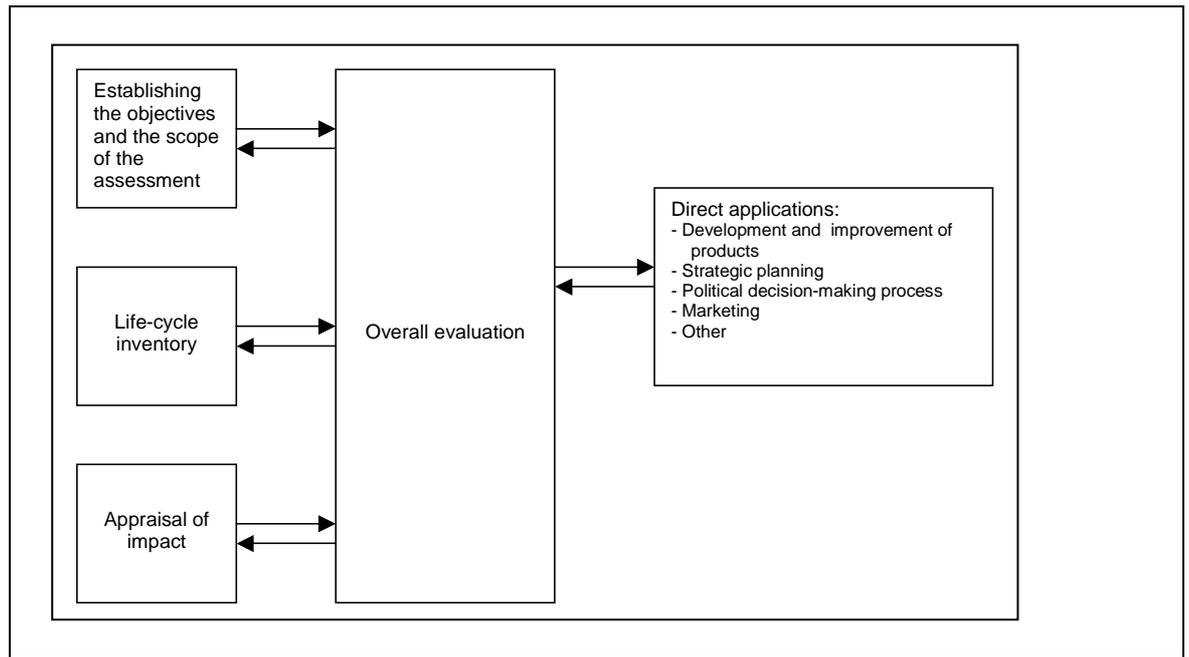
In order that specific nanotechnology applications can be assessed, a suite of appropriate methods must be selected that reflects the characteristic aspects of nanotechnology discussed in this publication. This will enable us to answer as fully as possible the various research questions being addressed.

## 1 The assessment concept

As the focus is on the prediction of potential environmental impacts, an appropriate starting point is the method known as life-cycle analysis (LCA). This is the most advanced and standardized procedure for appraising the environmental aspects associated with a product and predicting product-specific environmental impact. Unlike other existing methods, life-cycle analysis makes it possible to assess eco-efficiency potential. According to the EN ISO 14040 standard, a life-cycle analysis should consist of the following stages:

- Establishing the objectives and the scope of the assessment;
- Life-cycle inventory;
- Appraisal of impact; and
- Overall evaluation.

The following flow-chart clearly illustrates the interrelationships between these steps.



**Fig. 5: Stages involved in performing a life-cycle analysis**

Source: EN ISO 14040 1997

The arrows between the individual steps highlight the iterative nature of the procedure, with the outcome of a given step always being fed back into the preceding stage and resulting, if necessary, in the procedure being repeated.

The first stage is concerned with **establishing the objectives and the scope of the assessment**. The **life-cycle inventory** involves the gathering, compilation and analysis of data. As the name suggests, life-cycle analysis generally covers the entire life cycle of a product or service. Data on materials and energy have to be collated in physical units for each of these stages of the life cycle. On the input side, data are required on the consumption of raw and auxiliary materials and energy, and on the output side information is needed on products, air and water emissions and waste.

During the **impact appraisal** phase, the life-cycle inventory data are structured with regard to their ecological relevance (classification) and then pooled (characterization). In this way the resource consumption and emissions that occur over the course of the product life cycle are related to environmental impact, and these effects can then be discussed among experts and in the public arena.

The following table lists the impact categories and the various substances involved.

**Tab. 3: Impact categories and substances involved**

Source: Ankele; Steinfeldt 2002

Impact category	Substances involved and contributory factors
Utilization of re-sources	Consumption of renewable and non-renewable resources (crude oil, natural gas, coal, minerals, wood, etc.)
Greenhouse effect	Carbon dioxide (CO <sub>2</sub> ), methane (CH <sub>4</sub> ), nitrogen oxide (N <sub>2</sub> O) and others
Stratospheric ozone depletion	Chlorofluorocarbons (CFCs), brominated and halogenated hydrocarbons etc
Human toxicity	Volatile organic hydrocarbons (VOH), organic solvents, suspended particles, benzene, heavy-metal compounds (arsenic, cadmium, mercury, lead, nickel, etc.) sulphur dioxide (SO <sub>2</sub> ), nitrogen oxide (NO <sub>x</sub> ), fluoride, hydrogen fluoride, hydrogen chloride, carbon dioxide (CO), soot, etc.
Ecotoxicity	Sulphur dioxide (SO <sub>2</sub> ), nitrogen oxide (NO <sub>x</sub> ), fluoride, hydrogen fluoride, hydrogen chloride, lead (Pb), cadmium (Cd), copper (Cu), mercury (Hg), zinc (Zn), chromium (Cr), nickel (Ni), adsorbable organic halogens (AOX), etc
Summer smog	Nitrogen oxide (NO <sub>x</sub> ), methane (CH <sub>4</sub> ), volatile organic hydrocarbons (VOH), etc
Acidification	Sulphur dioxide (SO <sub>2</sub> ), nitrogen oxide (NO <sub>x</sub> ), ammonia (NH <sub>3</sub> ), hydrochloric acid (HCl), hydrogen fluoride (HF), etc
Aquatic eutrophication	Nitrate (NO <sub>3</sub> <sup>-</sup> ), ammonium (NH <sub>4</sub> <sup>+</sup> ), chemical oxygen demand (COD), total phosphorus, total nitrogen, etc.
Terrestrial eutrophication	Nitrogen oxide (NO <sub>x</sub> ), ammonia (NH <sub>3</sub> ), etc.
Use of natural spaces	Primary production (e.g. coal and ore mining), utilization (e.g. agriculture) of land of particular ecological value

The final step in life-cycle analysis is the **overall evaluation**. This involves drawing conclusions concerning the planned application(s), on the basis of which a concrete action plan is prepared. Given that the assessment concept needs to be comprehensive in scope, certain deficiencies in life-cycle analysis must be pointed out.

- Generally accepted impact models do not exist for all impact categories. This is especially the case for two highly important categories, namely human toxicity and ecotoxicity. For example, in terms of scale alone, it is not relevant to include fine-dust pollution (the label “PM<sub>10</sub> risk” identifies potential toxicity caused by particles under 10 µm in size) when life-cycle analysis is used for nanotechnology applications).
- In life-cycle analyses neither the risks nor the potency of applications are considered.

From our perspective, therefore, if an ecological assessment concept for nanotechnology applications is to be comprehensive, the following additional methods of assessment must be added to complement life-cycle analysis:

- Risk analysis;
- Toxicological analysis; and
- Analysis of intervention depth.

**Risk analysis** is the process which combines information about a particular situation (situational description, identification of hazards) with appraisal of risks that are based on possible consequences or hazards arising from alternative courses of action.

**Toxicological analysis** includes testing for acute toxicity, chronic toxicity, corrosive effects, skin and eye irritation, carcinogenic effects, sensitization (potential allergy-inducing effect), etc.

The notion of a technology's **depth of intervention** assesses the degree of "technical interference with control systems" in the natural environment, and how potent a technology is in terms of its impact and how far it extends the chains of cause and effect in space and time. This concept enables the "character" of a technology to be determined: in other words, the qualitative difference between, for instance, stoneworking and splitting the atom (see Gleich; Rubik 1996).

When a set of methods is put together in such a way, its focus must be adjusted to suit each different application context. This would allow environmental aspects associated with a given application to be appraised, and therefore – unlike other existing applications – make it possible to analyse potential eco-efficiency. It would also ensure that risk assessment incorporates the precautionary principle.

The following table is an attempt to portray the connections between the various nanospecific aspects/effects, the resulting problems, suitable methods of assessment and possible measures and requirements.

**Tab. 4: Connection between nano-specific aspects, suitable methods of assessment and possible measures**

Source: Steinfeld, IOEW

Aspect/effect	Problem	Method	Measure
Smallness	Ability to permeate (e.g. cell membranes)	Toxic analysis	Closed application, immobilization of particles, measurement techniques
Precision of the specification; purity, particle size	Product life-cycle costs; entropy	Life-cycle analysis	Eco-efficient production
Precision of the specification: rare materials	"New" materials in the environment (i.e. present in unprecedented quantities)	Life-cycle analysis, toxic analysis	Eco-efficient production, closed application
Specific ratio between surface area and volume	Mobilization, chemical reactivity	Toxic analysis, ototoxic analysis	Closed application, immobilization of particles
Self-organization	Uncontrollable autonomous development	Risk analysis, analysis of intervention depth	Inherent safety

## 2 Testing the assessment concept with reference to actual case studies

The practical applicability of this methodological concept is to be tested during the next phase of the project in follow-up case studies on specific processes or products (still to be selected) with the aim of drawing up ecological profiles. We are, however, aware that we are only able to use the methods of assessment described above - such as the life-cycle analysis laid down by the DIN ISO 14040 standard - as a general guide; we cannot comply with every single prescribed aspect. Based on our current level of knowledge, we can assume that the high standard of existing data required by a life-cycle analysis cannot be met by the follow-up case studies, since it can be assumed that the available data on a given product or process (and on others chosen for comparative purposes) will be incomplete and that it will not, owing to time and budget constraints, be possible to fill these gaps.<sup>18</sup>

Drawing up an ecological profile involves the following steps:

- Formulation of the framework conditions and definition of objectives for the relevant case study;
- Selection of other processes/products to be assessed for comparative purposes;
- Data collection and analysis of case studies (with a life-cycle inventory performed along the lines of the DIN ISO 14040 standard);
- Prediction of impact based on the DIN ISO 14040 standard;
- Analyses of, and/or discussions on, toxicity and risk
- Analysis of intervention depth; and
- Summary assessment of case studies.

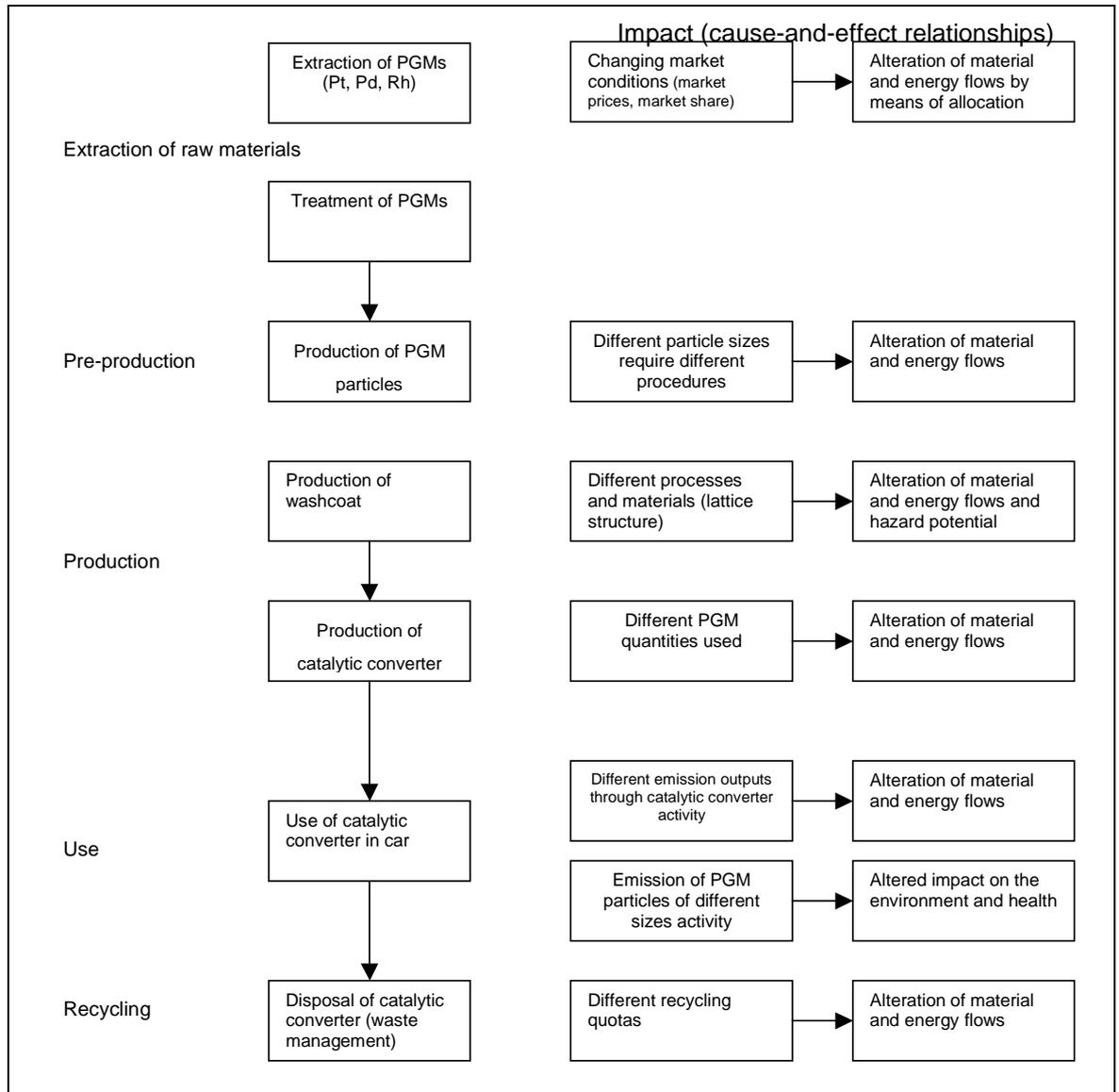
To specifically illustrate its applicability, the concept will now be outlined in more detail taking the example of **catalytic convertors in automobiles**. In a study for the Technology Assessment Bureau at the German parliament, the IOEW carried out initial work on drawing up ecoprofiles for nanotechnological applications (see Steinfeldt et al. 2002). The focal point of the case study on catalytic converters is on technological developments, characterized by the use of increasingly small nano-scale materials.

The case study restricted its focus to one area of application: the three-way catalytic converter. In a comparative investigation, based on the most influential parameters, five variations were looked at; these were chosen to reflect both the historical development of catalytic converter technology (see Hagelüken et al. 2001/Heck et al. 2002) and also – by including two more modern versions – the latest advances (see CSI 2002; Daihatsu News 2002). The ecological effects accompanying these developments were investigated.

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18 One approach to dealing with this problem is the method of simplified or streamlined LCA (see Christiansen et al. 1997 / Todd; Curran 1999).

The following flow-chart shows the full scope of the analysis. In addition, the impact (with cause-and-effect relationships) is indicated for each stage of the life cycle in relation to the use of precious metals.



**Fig. 6: Full scope of analysis for the catalytic converter and its impact, focusing on the use of platinum group metals (PGMs)**

Source: Steinfeldt et al. 2002

Even allowing for a number of gaps in the data (i.e. the yellow boxes on the chart) which may qualify the result, it is clear that in this particular application quantifiable ecological benefits are achieved. These relate to reduced emission of pollutants in car exhaust fumes and the lessened need for extraction of raw materials (platinum group metals, PGM), which is environmentally very costly. On the other hand, when it comes to assessing the potential hazard associated with PGM emissions, gaps in available knowledge leave a key question unresolved: whether the ever-diminishing size of nanoscale particles size gives rise to an additional combined effect. No substantive studies on this issue could be found in the literature.

Within the BMBF-project, the selection of examples aims on the one hand to cover in large extent the different ways of production as well as the spectrum of nanotechnology applications and basic physical structures. On the other hand we want to focus on selected priorities. As levels of selection and matching criteria we considered the following:

By type and extent of environmental impact:

- Expected eco-efficiency potential (high --- low)
- Possible risk and/or toxicity potential (high --- low)

By degree of “market-friendliness”:

- Blinndtext Blinndtext Blinndtext Blinndtext
- Market readiness (available now --- available in long term)
- Market relevance (high --- low)
- Possible spectrum of applications (wide --- narrow)

By level of innovation and amount of material turn over:

- Degree of innovation (low --- high).
- Expected amount of material turn over (high - - - low)

Out of the investigated nanotechnology applications we chose the following examples for our case studies:

1. Open applications of nanotechnology considering titanium oxide as example  
Main issue: discussion of possible risks and the toxicity potential
2. Nano-innovations within display sector  
Main issue: Estimation of the possible ecological efficiency potentials of energy or resource saving flat displays (OLED; FED) through a qualitative comparison with conventional products
3. Process innovation within the styrol synthesis  
Main issue: Description of ecological efficiency potentials of nanotechnology in a catalytic application by a comparing ecological profile
4. Nnoapplications within lights sector  
Main issue: Description of ecological efficiency potentials concerning energy-saving and long-life white LED's, quantum dots in comparison to the electric bulb
5. Eological efficiency of Nano-coatings  
Main issue: Description of ecological efficiency potentials of Nano-coatings by a comparing ecological profile

Tangible results from the case-study investigations will be available by the end of 2003.

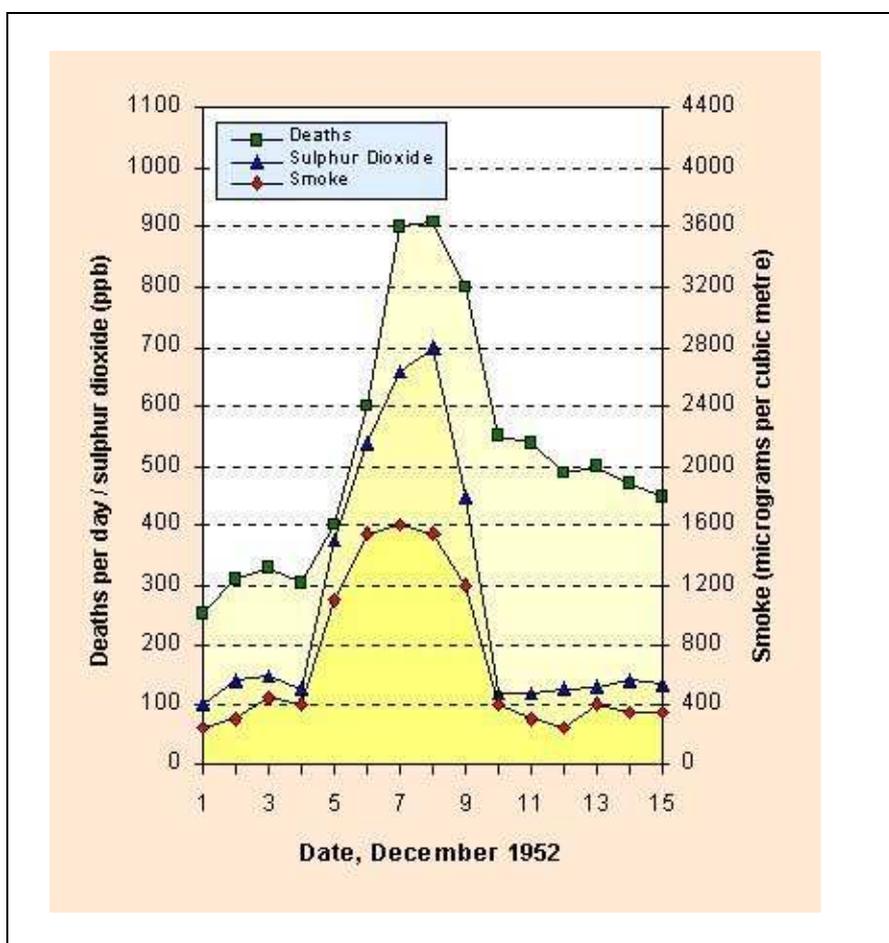
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# Toxicology of Nanoparticles

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It is a long known and well-studied fact that dusts at workplaces may lead to occupational diseases, e.g. pneumoconiosis of miners. But also high dust concentrations in the environment in combination with other air pollutants, such as sulphur oxides, nitrogen oxides, and carbon monoxide, repeatedly caused dramatic increases in mortality in the past, e.g. during the smog period in London at the beginning of December 1952 (Fig. 8, Schwartz, 1994). The rapid increase in air pollutants was followed by a drastic rise of mortality with a delay of one day. Deaths were mainly caused by diseases of the respiratory tract and the cardiovascular system.



**Fig. 7:** Dust and SO<sub>2</sub> concentrations as well as deaths per day as a function of time from 1st to 15th December 1952 in London.

Source:

[http://www.doc.mmu.ac.uk/aric/eae/Air\\_Quality/Older/Great\\_London\\_Smog.html](http://www.doc.mmu.ac.uk/aric/eae/Air_Quality/Older/Great_London_Smog.html)

Today, dust concentration in the environment has dropped to typically 20-30 µg/m<sup>3</sup> due to effective reduction measures taken by industry. Under smog conditions as prevailing at the beginning of January 2002, however, dust concentration measured as PM<sub>10</sub> (Particulate Matter < 10 µm) may

exceed  $150 \mu\text{g}/\text{m}^3$ . Worldwide epidemiological studies that were performed recently revealed that even such small dust concentrations are correlated with the frequency of illnesses and deaths (Tab. 4). These acute effects hardly occur in healthy persons, but above all in persons already suffering from serious cardiac and respiratory tract diseases (asthma, chronic bronchitis), small children, and elderly persons. A meta analysis demonstrates that an increase in  $\text{PM}_{10}$  concentration by  $10 \mu\text{g}/\text{m}^3$  is associated with an increase in mortality by about 1% (Thurston, 1996).

It is not yet clear how such small dust concentrations affect health. Among the causes discussed are various chemical aerosol components (metals, organic compounds, endotoxins) as well as physical properties, such as particle size. Anthropogenic components of environmental dusts mainly originate from burning processes. Due to exhaust air cleaning, they contain fine ( $< 1 \mu\text{m}$ ) and ultrafine particles (UFP,  $< 0.1 \mu\text{m}$ ) of small mass, but high particle number and an accordingly high surface area. These small particles may enter peripheral areas of the lung. They may initiate biological reactions or act as vehicles of other toxic components. Epidemiological studies made in the area of Erfurt (Wichmann et al., 2000) for the first time revealed a statistical correlation between mortality and UFP concentration.

Study area (reference)	Mean $\text{PM}_{10}$ ( $\mu\text{g}/\text{m}^3$ )	Maximum $\text{PM}_{10}$ ( $\mu\text{g}/\text{m}^3$ )	100 $\mu\text{g}/\text{m}^3$ RR	100 $\mu\text{g}/\text{m}^3$ (95%CI)
Utah Valley, UT (Pope et al., 1992)	47	297	1.16* 	(1.10-1.22)
St. Louis, MO (Dockery et al., 1992)	28	97	1.16* 	(1.01-1.33)
Kingston, TN (Dockery et al., 1992)	30	67	1.17* 	(0.88-1.57)
Birmingham, AL (Schwartz, 1993)	48	163	1.11* 	(1.02-1.20)
Athens, Greece (Touloumi et al., 1994)	78	306	1.07* 	(1.05-1.09)
Toronto, Canada (Özkaynak et al., 1994)	40	96	1.03** 	(1.00-1.06)
Los Angeles, CA (Kinney et al., 1995)	58	177	1.07* 	(1.05-1.09)
Chicago, IL (Ito, et al., 1995)	38	128	1.05** 	(1.03-1.07)
Santiago, Chile (Ostro et al., 1995)	115	367	1.05** 	(1.00-1.11)
			1.04** 	(0.98-1.09)
			1.05** 	(1.01-1.10)
			1.08* 	(1.06-1.12)
			1.15* 	(1.08-1.22)

\* Single pollutant model (i.e.,  $\text{PM}_{10}$ ).

\*\* Multiple-pollutant model (i.e.,  $\text{PM}_{10}$  and other pollutants simultaneously).

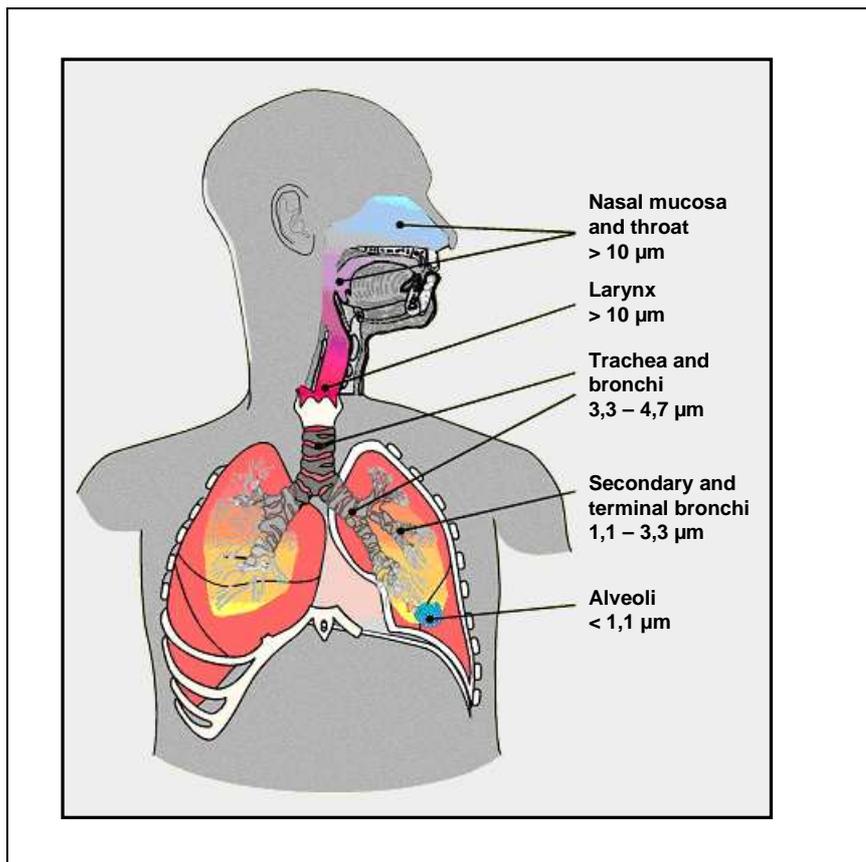
 One-day mean  $\text{PM}_{10}$  concentration employed.

 Multiple-day mean  $\text{PM}_{10}$  concentration employed.

**Fig. 8: Comparison of several epidemiological studies with respect to the relative risk (RR) of total mortality in case of an increase in the  $\text{PM}_{10}$  concentration by  $100 \mu\text{g}/\text{m}^3$**

Source: Thurston, 1996

The particle size determines which particles are inhaled and where they are deposited in the respiratory tract. Based on the experimental data available (Fig. 9), conventions with respect to the effect-related measurement of dust have been specified in DIN ISO 7708. The total inhalable fraction is approximated by  $\text{PM}_{10}$ , the fraction entering the alveoli by  $\text{PM}_{2.5}$  ( $< 2.5 \mu\text{m}$ ). In the European Union, an air quality regulation applies with  $\text{PM}_{10}$  equaling  $50 \mu\text{g}/\text{m}^3$  (annual mean). The American Environmental Protection Agency (EPA) recently adopted a new  $\text{PM}_{2.5}$  standard of  $25 \mu\text{g}/\text{m}^3$ .



**Fig. 9: Mean probability of suspended dust particles entering certain areas of the respiratory tract (separation efficiency)**

Source: according to DIN ISO 7708

# 1 Lung Damage by Inhaled Particles

In our respiratory system, various protection mechanisms serve to prevent damage from being caused by inhaled pathogens and foreign substances. Apart from mechanical removal (coughing, sneezing), unspecific and specific immunodefense processes and detoxification mechanisms play an important role. To control bacteria and viruses or to eliminate non-infectious particles, an inflammatory reaction is initiated locally by the immune cells existing there. In pulmonary alveoli, these are alveolar macrophages (Fig. 10). In addition to reactive oxygen species (ROS), proteins and lipids are released, which act as chemical messenger substances (mediators) on other cell types, e.g. epithelial cells lining the alveoli or endothelial cells lining the blood vessels in the direct vicinity. The starting destruction process of foreign matter also destroys healthy tissue that has to be repaired again by anti-inflammatory processes. By the fine regulation (homeostasis) of this network of mediators, damage of the lung or organism is limited. Subregulation or overregulation of certain mediators would cause increased damage and, hence, progressing illnesses.

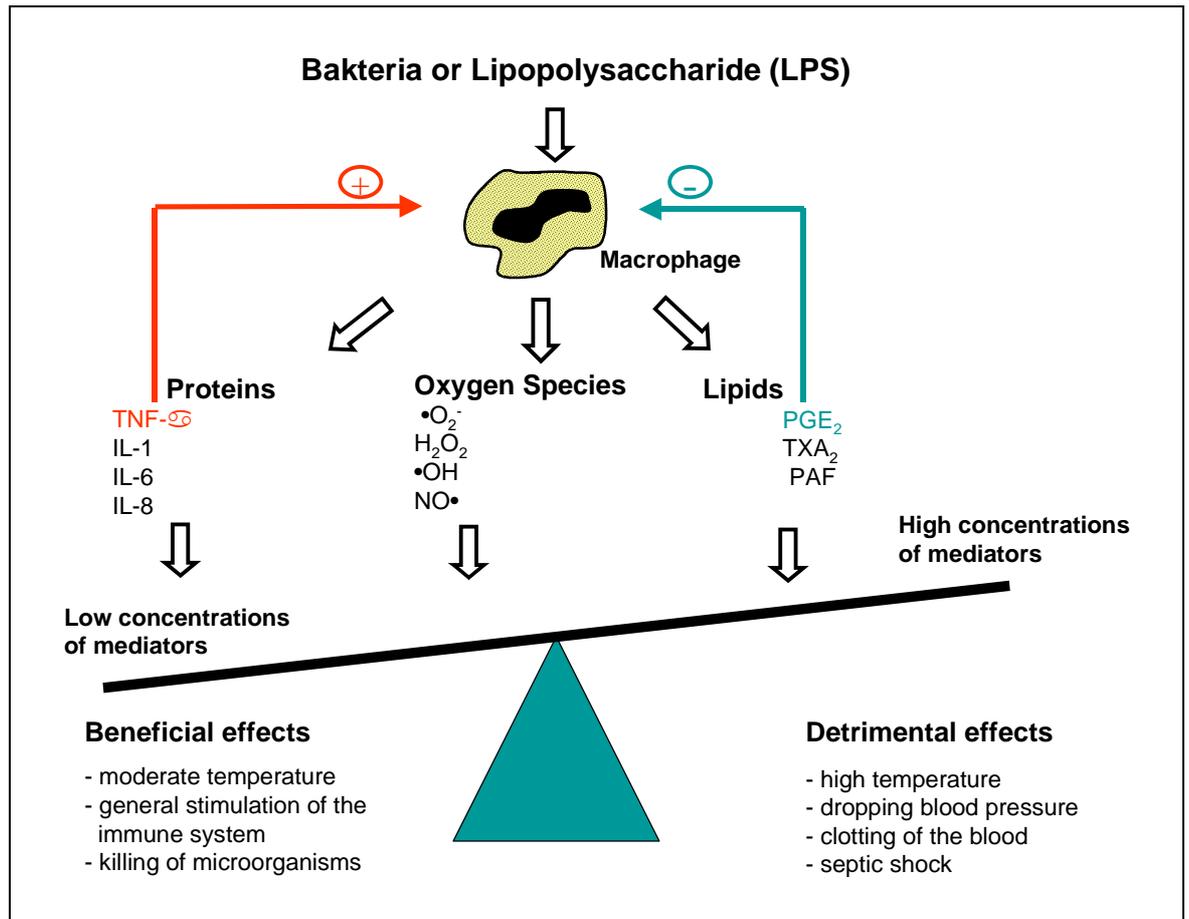


Fig. 10: LPS<sup>19</sup>

Inflammatory response to the inhalation of fine and ultrafine particles was studied extensively in man (Salvi et al., 1999, 2000) and animals (Review: Oberdörster, 2001). This response is characterised by invasion of inflammatory cells into the alveoli and is associated with the release of ROS and lysosomal enzymes, which damage the lung epithelium and, thus, reduce the capability of defending pathogens. The metal fraction of the environmental aerosol seems to play a crucial role in the initiation of PM-induced effects, as was revealed by a study combining experimental and epidemiological approaches (Ghio et al., 2000). Particles collected at various times in the Utah Valley, USA, were resuspended and instilled into the respiratory tract of healthy persons. Particles that had been collected during the operation phase of a local steel works exhibited a high metal concentration (among others, Fe, Cu, Zn, Pb, Ni) and induced a stronger inflammatory response than particles that had been collected during the decommissioning phase of the steel works and, hence, contained less metals.

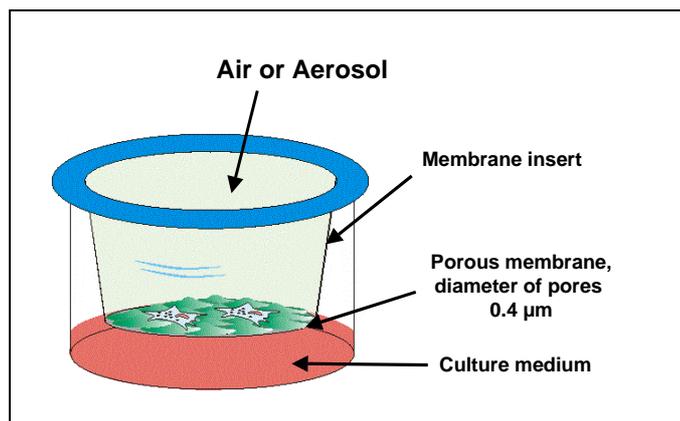
19 LPS (lipopolysaccharide) or certain bacteria stimulate macrophages to produce and release mediator molecules in the form of proteins (tumor necrosis factor- $\alpha$ , interleukines-1, -6, -8), reactive oxygen species (oxygen anion radical, hydrogen peroxide, hydroxy radical, nitrogen monoxide), and lipids (prostaglandin  $\text{E}_2$ , thromboxan  $\text{A}_2$ , platelet-activating factor). These so-called mediators are very sensitively adapted to each other and may initiate various beneficial or detrimental effects. The released substances partly have a retroactive effect on the macrophages. TNF- $\alpha$  increases the production of mediators (red arrow),  $\text{PGE}_2$  inhibits it (green arrow).

As a cause of the cytotoxic effect of particles, also surface properties and the electrokinetic potential of particles are discussed (Devlin et al., 2000). For instance, reactive siloxane bridges (Si-O-Si) and silanols (SiOH) are found on the surface of quartz particles. In the aqueous medium, the particles, through the negative charge of their surface, adsorb to surface proteins of cells. This results in the destruction of hydrogen bridge bonds, protein conformation is changed irreversibly, and lysis of the membrane takes place. By the coating of particles with positively charged organic molecules, e.g. dipalmitoyllecithin, proteins, immunoglobulines, or surfactant, the negative surface charge was reduced *in vitro* and, hence, the cytotoxic effect decreased. Quartz particles that were treated with aluminium lactate and instilled into rat lungs were found to be far less cytotoxic than untreated quartz particles (Duffin et al., 2001).

## 2 Work Performed at the Institute of Toxicology and Genetics

At the Institute of Toxicology and Genetics, lung-specific *in vitro* tests are carried out using an environmentally relevant aerosol to find out which chemical constituents and which particle size fractions contribute to the toxic effect. As an example of environmental particles, fly dust from a municipal waste incineration plant was selected, as the incineration process has already been studied in detail, similar to coal incineration, and as this issue is one of the main fields of work of the Research Center Karlsruhe (Paur et al., 2000).

In general, toxicity studies are carried out with cell cultures from the lung being treated with the particles to be studied submersedly in liquid culture media. In this respect, the dose refers to their concentration in the medium. For the investigation of particles, however, this test approach is hardly suited, as the physico-chemical properties of the particles and cell surfaces in the liquid phase differ from those of the gas phase. A close-to-reality model of the *in vivo* situation of the lung is the exposure of cells at the air/liquid barrier. However, the technical expenditure required is rather high, which is why the model is rarely used. On the one hand, a defined aerosol has to be generated and passed over the test cells in an appropriate manner. On the other hand, the cell cultures have to be kept viable over the test period by using appropriate carrier systems. Here, the cells were sown on a porous membrane (Fig. 11), as a result of which they can be supplied with liquid and nutrients through the pores during air exposure. Using this method, determination of dose-effect relations mostly is difficult, as the quantitative deposition of particles from the gas phase on the cells can only be calculated or estimated.



**Fig. 11:** Transwell® membrane system<sup>20</sup>

Following exposure, the viability of the cells is analysed and the culture medium is checked for its contents of released mediators that are characteristic of inflammatory responses. So far, we have succeeded in demonstrating that the method of resuspending fly ash in air and exposing lung cells via the atmosphere works in principle. Following the treatment of lung cells of human origin and of cells from the rat with particle suspensions in a submerged culture, ultrafine synthetic particles (Figs. 12 and 13) and fly ash particles (Fig. 14) were found to induce or enhance various parameters of an inflammatory response, e.g cytokine formation, in lung cells at non-cytotoxic concentrations already (Diabaté et al., 2002). These effects are possibly caused by the also proved formation of reactive oxygen species (ROS) due to fly ash exposure, as it is known that ROS interact with various signal transduction pathways that lead to the expression of cytokines.

<sup>20</sup> Transwell® membrane system for the exposure of cells at the air/liquid barrier. By the membrane insert, the system is divided into a lower and an upper compartment which are only connected via the pores in the membrane (diameter 0.4 μm). The pores are sufficiently large to allow particle, but not cell transfer between the compartments.

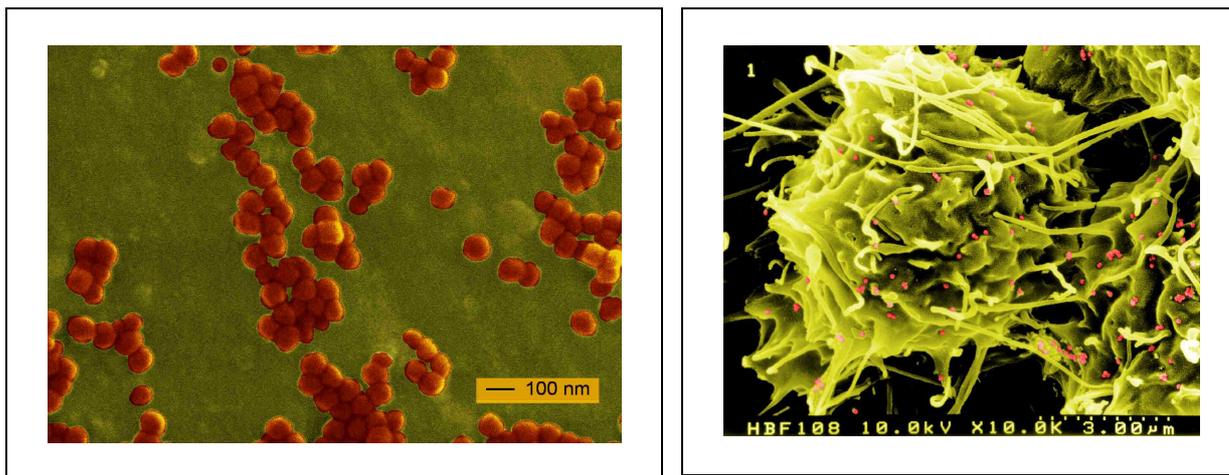


Fig. 12: Scanning electron microscopy of ultrafine particles.<sup>21</sup>

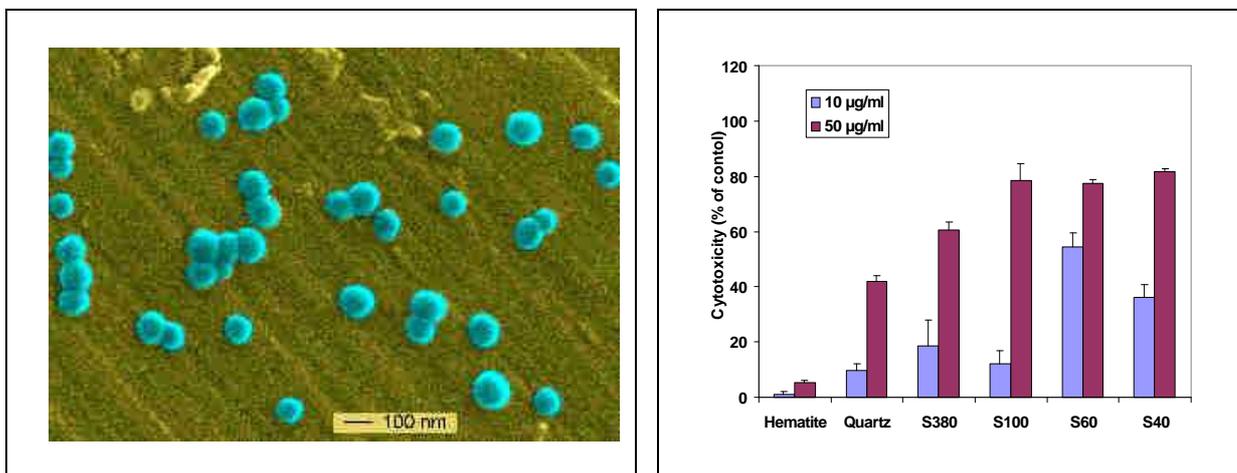
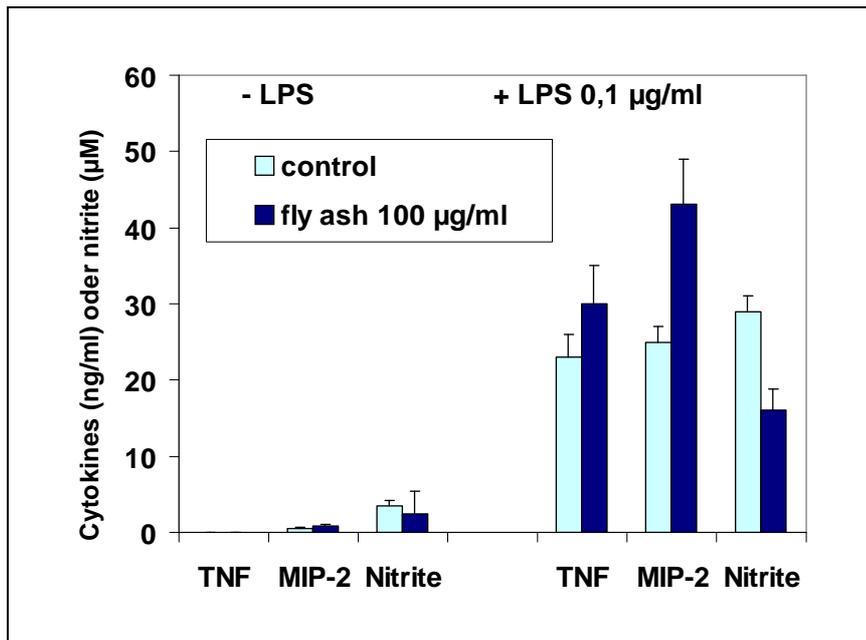


Fig. 13: Ultrafine particles and their cytotoxic effect..<sup>22</sup>

- 21 Left: representation of ultrafine hematite particles ( $\text{Fe}_2\text{O}_3$ , mean diameter 70 nm) synthesised by W. Ferstl (ITC-WGT) (microscopy by B. Neufang, HVT-HZ). Right: SEM (by H. Zöltzer, University of Kassel, Human Biology) of a macrophage of the mouse cell line RAW 264.7 (yellow), phagocytising hematite particles (red).
- 22 Left: scanning electron microscopy of ultrafine silicasol particles with a mean diameter of 60 nm (B. Neufang, HVT-HZ). Right: measurement of the cytotoxicity of hematite ( $\alpha\text{-Fe}_2\text{O}_3$ , ~ 70 nm) and silicasol (amorphous  $\text{SiO}_2$ : 380, 100, 60, and 40 nm in diameter) (both synthesised by W. Ferstl, ITC-WGT) as well as of quartz dust (< 5  $\mu\text{m}$ ) in mouse macrophages (RAW 234.7). The smaller silicasol particles are more toxic than the large ones. In contrast to this, hematite of about the same size is practically non-toxic.



**Fig. 14: LPS-stimulated alveolar macrophages**

LPS-stimulated alveolar macrophages of the rat (NR8383) react to the subtoxic fly ash concentration of 100 µg/ml with an enhanced release of the cytokines TNF- $\alpha$  and MIP-2 as well as with a reduced formation of NO, measured as nitrite. In unstimulated cells (-LPS) these inflammatory parameters are not affected by fly ash (Diabaté et al., 2002)

The results obtained from the studies described shall be used to assess effects of particulate air pollutions from different sources on health and to take specific emission reduction measures. It is of equal importance to assess particle emissions that may result from the use of new technologies or new fuels so as to steer developments in the right direction or decide on a more extended use as early as possible.

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