The case of nanobiotechnology

Towards a prospective risk assessment

Armin Grunwald

Scientific progress and technical innovations are necessary not only to raise, or at least to secure, our present level of prosperity and to ensure competitiveness in the global market, but also to progress further in medicine and sustainable development. On these points there is, to a great extent, consensus. Scientific and technical progress, however, do not produce only positive outcomes. New technologies have unintended side effects, such as hazards to the natural environment, to human health or to society at large. The ozone hole, the long unrecognized carcinogenic effects of asbestos and catastrophic accidents, such as Bhopal or Chernobyl, are well-known examples (Harremoes *et al*, 2002). This ambivalence of science and technology is largely acknowledged today, and has led to risk research, technology assessment and ethical reflection to anticipate, counter and minimize the negative effects (Grunwald, 2002).

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But there are still considerable differences in the public acceptance of research and new technologies and their potential risks: "The core problem...is the ongoing conflict between those who embrace the changes that come with new vistas of research and those who loathe and dread them" (Gannon, 2003). Basically, the public debate about new technologies is characterized by these two extreme positions. On one side are the technology sceptics,

who exclusively look at the risks, expect mainly negative effects from technological progress and demand 'zero risk' for all new technologies. On the opposite side are the technology optimists, who—in conformity with the once prevalent optimistic belief in progress—expect mainly positive effects from technology and demand that 'residual risk' must be accepted. I find both extremes exaggerated and one-sided, and I believe that both standpoints are, in the long run, detrimental to scientific and technological progress and their acceptance in society. This idea will probably come as no surprise in regard to the position of the technology sceptics; after all, it is their intention to counter or slow technological progress. In this article, I explain why, in my opinion, the technology optimists are also a hindrance to scientific and technological progress, and its implementation, when they put forward their arguments in a particular way.

Among economists, and also among many scientists, it is quite unpopular to consider or even to talk about the potential risks of new technologies. Such an attitude of denial has arisen out of fear of the eternal pessimists and the enemies of technology. Indeed, sceptics have often successfully mobilized public opinion against innovative technologies by means of campaigns and spectacular public events or demonstrations. Under public pressure, politicians have been coerced into delaying scientific and technical progress through regulation or restructuring of research funding, often in the name of an extensively interpreted precautionary principle. In this manner, it is increasingly

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hard to make early use of new technologies to increase prosperity or to find cures for diseases.

There have been some examples of this, but there have also been developments that took the reverse path: early and extensive use of a new technology without thorough investigation of the risks, ignorance of the first cases of disease or of environmental problems, trivializing statements from scientists and industry, and slow reactions from policy makers and regulators (Harremoes *et al*, 2002). The result was not only a great deal of human suffering and economic loss, but also often marked the end of the technology that caused the problems. The example of asbestos is, in this respect, a unique warning, but there are many other cases in which risks were first denied, then played down and eventually—often far too late—openly admitted. This is the classical history of many incidents in the chemical industry or in nuclear power production. Public confidence in the ability of science and technology to deal with risks is not necessarily developed in such a fashion; on the contrary, this form of risk management immediately destroys any trust that has been painstakingly built up. Instead, early and open discussion of possible technological risks contributes, in the medium and long term, towards upholding and strengthening confidence in science and technology.

Nanoflower bouquet. These images show complex structures formed from silicon carbide nanowires grown from a vapour phase. During the growth process the nanowires fuse together to form the intricate 3D structures visible. By simply varying the growth conditions, the morphology of the resultant films can be precisely controlled. Images courtesy of Ghim Wei Ho and Professor Mark E Welland, Nanoscience Centre, University of Cambridge, UK.

The lessons learned from past accidents also apply to new technologies. It is generally true that innovative technology can always be connected to risks, early knowledge of which is, in fact, desirable but is possible to only a limited extent. Trying to ignore or conceal this would backfire at some point, because these risks would inevitably be discovered and made public in an open society. Declaring technological risks to be non-existent is possible only in totalitarian states—as was actually the practice in Communist nations, in which no mishaps or environmental problems officially existed. If such risks are discovered in the later phase of technological development, moderate correction is no longer possible. Often, all that remains is the complete abandonment of the technology in question, good examples being the chlorofluorinated

hydrocarbons in refrigerators, and—again—asbestos. Early consideration of their risks and correspondingly careful management could have helped to avoid the serious negative consequences, and possibly would have saved products, businesses and jobs.

There are pertinent cases, not in which excessive discussion of risks was detrimental, but rather where the ignorance or lack of knowledge of risks caused disastrous consequences. Consequently, promises of the positive effects of technological progress, which ignore technology's ambivalence, collapse when this ambivalence becomes apparent—particularly when risks to health or to the natural environment appear. In this manner, those who ignore the existence of technological hazards are playing directly into the hands of the technology sceptics.

If, conversely, one proceeds carefully from the beginning, neither exaggerating nor denying potential risks, but addressing them openly and trying to analyse them through research, then subsequent disappointment and loss of confidence can be prevented. If it is openly acknowledged that implementing new technologies might cause risks, then the mere possibility of risk can no longer be used as an argument for stopping technological progress. In particular, the awareness of potential risks does not legitimize the calls for a moratorium. Risks are so evidently connected with technology that no argument against technology can be derived from their possibility. To this end, a more detailed investigation is necessary: how great are the risks, what types of risks exist, what possible damage could occur, and what is the relationship of these risks to the expected benefit?

Technology is developed with an eye to the future: to meet a presumed need, tackle emerging problems or create new markets. These anticipated effects are essential elements for decision making during the development of a new technology. They include the intended effects—that is, the purpose and function of a technology and the goals for which it is developed—and the unintended effects or 'side effects', including misappropriation and abuse. Independently of these deliberations is the differentiation between the societal desirability of new technologies and their undesirability: society may reject intended effects, just as side effects can eventually be perceived as positive or acceptable. Technological risks clearly belong to the unintended and undesirable side effects.

We also have to take into account the 'proximity' of these effects: immediate or primary effects are direct consequences of the application of a technology and are inseparable from its use. The expulsion of combustion residues by a jet turbine belongs in this category. The more problematic aspects of the effects of technology, however, concern the indirect or secondary effects, which spread by way of various and insufficiently known cause-effect relationships. Referring to the example above, combustion residues have an impact on the climate and the Earth's atmosphere. In general, secondary effects are a result of the direct effects of any

technology on the natural environment, on humanity and on society.

Technological risks are a subset of these secondary effects (Grunwald, 2002), which can be placed in four main groups: risk of accidents; risks to health; risks to the environment; and social risks. Accidents in technical facilities are disruptions of normal operation. Above all, incidents in nuclear power plants—Three Mile Island in 1979 and Chernobyl in 1986—lastingly shattered public confidence in this method of producing energy, but also fundamentally disrupted public trust in the technology itself and in the experts and politicians supporting it. Similarly, the poisonous gas catastrophes in Seveso, Italy, and Bhopal, India, highlighted the extreme dangers of certain chemical production plants.

The use of a new technology may also lead to emissions or products that can affect human health. The known risks and side effects of medicines—for example, the Lipobay® affair—and also the dramatic history of asbestos belong in this category. Entire chapters of occupational laws and regulations are direct reactions to health problems caused by new products and technologies.

Similarly, effects on the natural environment, such as air pollution, the ozone hole, and chemical residues in ground water and in the soil, are well-known unintended consequences of technology. Other than accidents in technical facilities, these are often gradual processes. They are not always easily recognizable, and there is dissent on the question of tolerance limits, or cut-off or threshold values, beyond which protective or remedial measures would have to be taken.

Social and cultural effects of technology—such as the loss of jobs through rationalization and automation—particularly affect less-qualified labour. Further risks might also include potential misuse: for instance, modern surveillance technologies can now be used to listen in on fixed network or mobile telephone conversations, to track internet users, to video monitor public places and to analyse the genetic traits of population groups. Large segments of the population indeed consider ethical ‘slippery slopes’ in biomedical research as ‘cultural’ risks.

The terrorist attacks on 11 September 2001 have drawn our attention to a completely new type of technological risk,

namely, its intentional misappropriation and misuse. This is neither a case of gradual side effects nor of accidents, but a redefinition of the purposes of technology. Modification of chemical plants for the production of toxic agents or of biological laboratories for breeding anthrax pathogens, and the misuse of uranium isotopes intended for nuclear power plants to make nuclear weapons, are examples in this category.

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Technological risks have several innate characteristics, which are important factors in risk research and risk assessment. These are, in particular: spatially far-reaching effects, such as emissions into the atmosphere or the global water cycle; the temporal

scope of consequences, the classical example being the disposal of radioactive wastes, which will require careful observation for thousands of years; and the potential scope of a problem if both present and future populations will be affected. Other characteristics are: delayed effects, when perceptible damage appears only decades after its cause—for example, the ozone hole or the carcinogenic effects of asbestos (Harremoes *et al*, 2002)—and difficulties in ascertaining a causal chain, as initially occurred with the first cases of mad cow disease in the UK. Poor or insufficient perceptibility of risks—human sensory organs cannot measure radioactivity, for instance—can further increase the public’s negative attitude. Another characteristic is society’s vulnerability to technical dysfunction, which we witnessed last year when large parts of the electricity grid in Northeast USA and Canada broke down. Furthermore, risks can cause irreversible damage—genetically manipulated organisms, once released, may never be completely retrieved from the natural

Nanotrees

environment. These risk characteristics are often compounded by a lack of, or a diffuse distribution of, responsibility and the fact that we cannot predict precisely whether an event will happen or damage will occur, but can only express their likelihood in terms of (often uncertain) probabilities.

In several instances in the past, side effects interfered with or even counteracted the actual goals pursued by means of technology. This ambivalence of technology, the discrepancy between the intended and the realized effects, constitutes a *conditio humana* of technological civilization. Consequently, the demand for 'zero risk', as well as disregarding or denying the 'dark side' of technology, are both senseless positions. The challenge instead is in addressing the risks, in analysing and evaluating them by taking into account the expected benefits, and in considering these deliberations in the decision-making process.

In recent years, we have seen a new debate emerging about the risks of nanotechnology, a new field of research that has drawn considerable scientific, political and public interest. The possibility of controlling matter at the molecular and atomic level for further miniaturization of components, products and methods, and the prospect of building new products atom-by-atom even to the extent of 'nanomachines', are fascinating and present far-reaching possibilities for application. In addition to the usual definition of nanotechnology (Schmid *et al.*, 2003), nanobiotechnology makes additional use of biological components to design and construct machinery at the molecular level (VDI, 2002). Here, one distinguishes between 'Nano2Bio', which uses nanotechnology for the analysis and production of biological nanosystems, and 'Bio2Nano', which uses biotic materials and structures to build technical nanosystems. The rationale for this nanobiotechnology approach is that basic life processes take place on the nano-scale, because this is the size of proteins, which take care of most cellular processes. Cellular structures, such as mitochondria and transport vesicles that have an essential role in cellular metabolism, could thus become building elements for bio-nanomachines. Nanobiotechnology could thus make cellular engineering possible, by designing living cells to perform certain tasks, produce specific molecules or link biological processes with man-made

Nanoflower

technology, such as computer chips, and in this way enable scientists to control them (Roco & Bainbridge, 2002). Biological molecules could act as light-gathering and light-transforming components, signal converters, catalysts, pumps or motors in nanomachines to produce energy or specific products, perform monitoring tasks or store data. Nanobiotechnology extends the language of engineering, as it was applied in biotechnology to biological systems, to the nano-level: "The fact that biological processes are in a way dependent on molecular machines and clearly defined structures shows that building new nanomachines is physically possible" (Kralj & Pavelic, 2003).

First applications of this technology would come in analytical chemistry and medical diagnosis, the production of bioactive substances, the targeted transport of drugs within the human body or the production of biocompatible materials and surfaces. In fact, medicine will probably make wider use of nanotechnology first. "Although many of the ideas developed in nanomedicine might seem to be in the realm of science fiction, only a few more steps are needed to make them come true, so the 'time-to-market' of these technologies will not be as long as it seems today. Nanotechnology will soon allow many diseases to be monitored, diagnosed and treated in a minimally invasive way, and it thus holds great promise for improving health and prolonging life. Whereas molecular or personalized medicine will bring better diagnosis and prevention of disease, nanomedicine might very well be the next breakthrough in the treatment of disease" (Kralj & Pavelic, 2003).

Using nanotechnology-based diagnostic instruments, physicians could detect diseases or predispositions to diseases much earlier than at present, while 'lab-on-a-chip' technology could further promote personalized medicine. Nanotechnology could help to develop new therapies that are free of side effects or could improve the biocompatibility of artificial implants. As a qualifier, however, it should be noted that most of these positive effects of nanotechnology on human health are, so far, primarily hypothetical.

The potential is so remarkable that ethical reflection almost seems to be superfluous—if one looks solely at the benefits. But a comprehensive analysis has to include possible risks as well. Let me note at this point that medicine is probably best suited to deal with this new technology, which may harbour as yet unknown hazards. There is no other research field in which dealing with risks is so natural and so reliable as in medicine and pharmaceuticals. It is self-evident that any new treatment or method involves risks, and medical research has accordingly evolved rigorous risk-assessment procedures. Furthermore, the testing and approval of new medicines and treatments is closely regulated by government agencies that have constantly been raising the safety thresholds for new drug approvals.

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However, the feared risks of nanobiotechnological innovations have little to do with foreseeable applications such as those described above. They rather concern the 'visionary' and speculative applications. US author Michael Crichton, in his novel *Prey*, might well have triggered some of these fears in his story about a swarm of nanorobots, developed for the military, that evolve on their own while feeding on their human creators. More seriously, critics fear that nanoparticles, due to their submicroscopic size, could invade the human body unhindered and cause unforeseeable effects, or that

self-replicating robots could multiply out of control (Joy, 2000). The ability to combine biological material with man-made technology also raises warnings against human presumptuousness in trying to overcome the physical or psychological barriers put up by nature (Roco & Bainbridge, 2002) and against using nanotechnology to blur the boundaries between humans and technology. More generally—and as with any new technology—critics also point to a ‘nano-divide’, a division of global society into the people, groups or nations who will profit from the new technology and those who will not be able to afford it (Fleischer, 2003). It should also be considered that the extreme expectations at present can themselves become a risk, namely, if they are not realized within the foreseeable future. Disappointed hopes can swing the pendulum to the other extreme and reduce the interest of politics and the economy in promoting further research in this field.

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One could reply that these speculations belong in the realm of science fiction rather than in serious risk analysis (Gannon, 2003). That may well be so. Nonetheless, it is not only sensible but, in fact, necessary to consider the speculative risks of nanobiotechnology. Even if these assertions are mere speculations, they often have, through public debate, real effects on society, public perception and public opinion. A critical discussion of the negative utopias would therefore be an important contribution to any rational discussion of the benefits and hazards of nanotechnology.

The further development of nanobiotechnology must therefore be accompanied by continuous research on possible risks and its ethical and political implications. First and foremost, it requires a

prospective technology assessment of current opportunities and risks (Grunwald, 2002) and constant monitoring of the state of the art for new opportunities and risks as well as the conditions under which they can become reality. As mentioned above, a ‘vision assessment’ (Grin & Grunwald, 2000) would investigate the positive and negative utopias. All of these would eventually lead to an open dialogue with the participation of nanobiotechnologists, the medical profession and people specialized in technology assessment.

If the premise of this article—that risks are inseparably connected to new technologies—is correct, then the development and implementation of new technologies can be described metaphorically as an ‘experiment’. Experiments are carefully planned, but the results cannot be anticipated, despite good predictions. In the same sense, the introduction of a new technology in society shows experimental aspects: its development and implementation can be carefully planned beforehand considering current scientific knowledge, but its results can neither be predicted nor determined. Uncertainties and risks remain.

The question then arises, how such ‘experiments’ can be carried out as responsibly and as legitimately as possible. Science, technology and technology assessment first have to take care that the ‘experiments’ are as well planned as possible through analyses of the situation, through innovative technology, modelling and simulation. It also requires constantly assessing the painstaking performance of the ‘experiment’ while observing the effects of implementation, comparing the results with the goals pursued and investigating the causes of deviations. This is precisely the principle of long-term monitoring, which explicitly acknowledges the incomplete and uncertain knowledge of the effects of technology, as well as the possible existence of risks, and draws the corresponding conclusions. In this ‘experimental’ situation, it is important to grasp every opportunity for learning. This means

that the introduction of technology is an open process, during which new experiences co-determine the future course. In this sense, an accompanying, prospective risk assessment is an indispensable element of the responsible development of nanobiotechnology.

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Armin Grunwald is Director of the Institute of Technology Assessment and Systems Analysis (ITAS) at the Research Centre Karlsruhe, Germany.

E-mail: armin.grunwald@itas.fzk.de

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