How big can small actually be?

How big can small actually be?

Some remarks on research at the nanometre scale and the potential consequences of nanotechnology

Study Group on the Consequences of Nanotechnology

Royal Netherlands Academy of Arts and Sciences
Amsterdam, November 2004

P.O. Box 19121, 1000 GC Amsterdam, the Netherlands
T + 31 20 551 07 00
F + 31 20 620 49 41
E knaw@bureau.knaw.nl
www.knaw.nl

ISBN 90-6984-431-1

The paper in this publication meets the requirements of ∞ iso-norm 9706 (1994) for permanence.

Koninklijke
Nederlandse
Akademie van
Wetenschappen

Foreword

At the request of the Dutch Minister of Education, Culture and Science, the Royal Netherlands Academy of Arts and Sciences (KNAW) has surveyed the potential societal and ethical implications of nanoscience and nanotechnology.

An Academy study group made up of researchers concludes that nanoscience constitutes an interesting and useful development in the modern natural sciences. Speculation in a number of publications regarding self-replicating minimachines can be dismissed as entirely unrealistic. The Dutch government should provide support for nanoscience and nanotechnology (this is in fact being done already).

The Academy study group believes that additional research is necessary to determine the degradability of some nanoparticles in the environment and the toxicity of both stable nanoparticles and the residues left behind when degradable nanoparticles break down. Once it has been clarified which regulations are necessary to minimize harmful effects on health and the environment, these can be embedded within the existing framework of environmental and health legislation. In this respect, coordination with the relevant EU regulations is essential.

Prof. W.J.M. Levelt,
President
Royal Netherlands Academy of Arts and Sciences

Contents

1 Introduction

The results of much scientific research are never mentioned in the newspapers, but there also is research that researchers and the public cannot get enough of. One branch of science that is currently the object of increasing public attention is nanoscience and nanotechnology. These disciplines involve studying and constructing objects on a length scale of from 1 to 100 nanometres; in other words, one is dealing with individual atoms and molecules. It is now possible for the first time to carry out research at such a detailed level on individual components of material and to combine them with extreme precision into larger entities. This is an important development from the point of view of potential applications and a great deal is therefore expected from nanoscience and nanotechnology in a wide range of fields, from medicine to materials science.

Although it may produce tangible results, the actual research takes place largely out of the public eye. Understanding it requires specialised knowledge, and it also takes place in laboratories, where most people are unaware of it. As a result, a lack of understanding of the development possibilities and of possible undesirable applications may lead to disquiet. A few decades ago, for example, there was public concern regarding the application of results of nuclear physics to energy conversion. More recently, people have become worried about the conscious and deliberate alteration of the genetic material of living creatures.

In many cases, that concern is unwarranted. But public concern does demand that research and its consequences be explained. Researchers should not only put their efforts into carrying out research programmes but also into informing the general public about their research and its potential consequences, this may not always be sufficient to remove public concern. It is also important for the public to be able to have its say about the desirability of the research and the way in which the knowledge gained may – or may not – be applied.

Nanoscience research can make an enormous contribution to the knowledge-based economy. For the Netherlands, developing new knowledge and applying it in a responsible manner are essential for our well-being and welfare and for maintaining a good position within Europe. At the same time, there remain many things that some believe will become possible in the future but which experts are convinced are in fact impossible. It is therefore important to rebut exaggerated expectations and to dispose of unjustified concerns. It is useful to explain which of the dangers predicted for the future are realistic so as to be able to take necessary measures in good time.

Comparison of dimensions of various objects	
diameter of pinhead	1 millimetre, or 1 million nanometres
diameter of human hair	80 micrometres, or 80,000 nanometres
length of tail of human sperm cell	50 micrometres
diameter of human egg cell (ovum)	20 micrometres
thickness of aluminium kitchen foil	10 micrometres
diameter of bacterium	2 micrometres
thickness of wall of soap bubble	750 nanometres
length of virus	100 nanometres
thickness of DNA molecule	2 nanometres
diameter of hydrogen atom	0.1 nanometres

Although public concern about potential dangers of nanotechnology would seem to be unjustified, research has in fact shown that some nanoparticles can have an adverse effect on health and the environment. The Minister of Education, Culture and Science, Maria van der Hoeven, therefore considers it important for there to be discussion of nanoscience and nanotechnology. In order to facilitate such discussion, she has requested the Royal Netherlands Academy of Arts and Sciences (KNAW) to draw up a report on current and future consequences for society of nanotechnology and its ethical ramifications.[1] This memorandum, drawn up by KNAW's Study Group on the Consequences of Nanotechnology, comprises a brief initial response to the Minister's request. KNAW has also commented on the study recently published by the Royal Society and the Royal Academy of Engineering regarding the effects of nanotechnology, and the potential implications of that report for nanoscience and nanotechnology in the Netherlands.

The present memorandum first looks at various reasons for scientific interest in nanotechnology (2.1). It then goes on to deal with a number of definitions of nanoscience and nanotechnology (2.2). Some nanoparticles may have an adverse effect on human health and the environment; proposals are made for a suitable approach to this problem (3.1). Nanotechnology is sometimes seen as hazardous because of the supposed uncontrolled replication of 'nanobots'. An explanation of the impossibility of this scenario is discussed in 3.2.

Nanotechnology deals primarily with inanimate nature, but it does have common ground with biotechnology (3.3). For ethical and societal reasons, nanoscience and nanotechnology should be subject to the principles of precaution and proportionality. The need for a balance between these principles and the conclusion regarding the toxic effects of nanoparticles lead to a recommendation that research plans should be subject to careful assessment. A suitable

[1] Letter dated 8 August 2003 from the Minister of Education, Culture and Science to KNAW.

system of regulation means that safety monitoring will be possible for both industrial production processes and research institutions (3.4). This memorandum ends with some conclusions and recommendations (4).

2 Nanoscience and nanotechnology

2.1 New research

‘nano’ comes from the Greek word ‘*nanos*’, meaning a dwarf. Like ‘mega’, ‘kilo’, or ‘micro’, it refers to an order of magnitude, in this case to a billionth part of something; a nanometre is therefore one billionth of a metre and a nanosecond is one billionth of a second. The terms ‘nanoscience’ and ‘nanotechnology’ simply mean that objects are studied or manipulated with dimensions of between 1 and 100 billionths of a metre, i.e. ‘nanometres’.

Nanoscience and nanotechnology are exciting to scientists for a number of reasons, four in particular. The *first* of these concerns the production of materials and objects. Basically, two contrasting methods are used. One of them involves starting with a quantity of material and removing what is unnecessary. This ‘top-down’ method makes it possible to construct increasingly tiny structures. Ongoing technological advances allow ever-smaller objects to be produced, or objects with increasingly accurate specifications. This approach is particularly significant when producing computer components by means of lithography. Reducing the size of components and mounting them closer to one another allows us to boost the speed at which computers operate. Just what the limit is for this technology is the subject of much discussion.[2] Top-down techniques of this kind are gradually enabling removing individual atoms from a larger object.

The other method is based on bringing raw materials together and causing them to interact. Until recently, this ‘bottom-up’ method only allowed substances to react with one another in stages. The atoms and molecules in each of the substances could form bonds, thus producing a new substance. Which individual atoms or molecules reacted with one another had to be left to chance. Recently, however, it has become possible to manipulate molecules so that structures can be produced according to a previously determined plan; this advance has unprecedented consequences for the properties of the objects and materials thus constructed.

The diameter of the Earth is 12,756 kilometres. The diameter of a ‘buckyball’ – a football-shaped structure consisting of 60 carbon atoms – is 0.7 nanometres. A ball with a diameter of 9.5 centimetres is as much smaller than the Earth than it is larger than a buckyball (a soccer ball has a diameter of 22 centimetres and a tennis ball 6.7 centimetres).

The advent of *scanning tunnelling* microscopy and *atomic force* microscopy has made it possible to observe and manipulate individual atoms. The micro-

[2] Gordon Moore predicted in 1965 that the processing capacity of computers would increase exponentially, doubling every 18 to 24 months. This prediction is sometimes referred to as ‘Moore’s law’. It seems we will soon reach the limits of the interval predicted by Moore. After all, each of the smallest components of a computer still consists of large numbers of atoms. And even though components are now being designed that consist of only a few atoms, it is not possible to construct computer components consisting of only part of an atom.

scopes involved do not make use of light within the visible spectrum; objects of nanometre size are in fact much smaller than the wavelengths of visible light. In order to 'see' such objects, a tiny needle is used to scan the surface. These 'bottom-up' techniques are primarily important in chemistry and biology; in fact, we can now 'treat' individual atoms and cause them to interact with one another. The top-down and the bottom-up methods have now converged in the investigation and construction of objects measurable in nanometres. One of the results is that researchers from different disciplines are starting to collaborate in this new field of research, making major advances possible.

The *second* reason for nanoscience being the object of scientific interest has to do with fundamental properties of matter. Since the development of quantum mechanics in the 1920s and 30s, it is known – in theory – that the properties of substances as we can observe them differ greatly from those of individual atoms or molecules of the same substances. A single, isolated iron atom, for example, behaves very differently to the millions of atoms making up the tiniest observable iron filing. This is due to the change in physical properties resulting from quantum confinement. In other words, if there is a great deal of space relative to the dimensions of the atoms, the material has the properties we are familiar with; in individual atoms, however, the properties of the material are determined far more by the mobility of the electrons that create the bonds between the atoms. Nanoscience makes it possible to actually observe the behaviour of materials that used only to be known about in theory. To take an example: silicon – the main component of sand – is not luminous, but quantum confinement causes nanoparticles of silicon in fact to emit light. In silicon nanoparticles, the space the electrons have in which to move is no more than a few times the size of a silicon atom. This restriction on their mobility leads, in the case of silicon, to different optical properties, a phenomenon with major potential consequences for the ICT industry.

Thirdly, chemical properties depend on the ratio of the surface area to the volume of the particles concerned. When objects get smaller, their volume is reduced to a much greater extent than their surface area. In objects with macroscopic dimensions, properties associated with the volume play a much greater role than those associated with the surface area of the object. However, at a scale of just a few up to a few tens of nanometres, surface properties are predominant. This surface effect is also one reason why individual particles at nanometre scale display entirely different properties to particles with dimensions of micrometres or millimetres.

Researchers are interested in this effect partly because of its potential applications. In the chemical industry, for example, many conversion processes take place only slowly. Adding heat can accelerate them, but heating consumes a great deal of energy; it also has a negative effect on some compounds. In such cases, one solution is to use a catalyst. A catalyst works by interacting with another molecule; the interaction takes place on the surface of the catalyst. The larger the surface area, the more efficient is the process and the smaller the quantity of catalyst that needs to be used. One can ensure that the surface area is larger either by using more of the catalyst or by reducing the size of the particles so that more of the total content of a particle is located on its exterior. Combining this with other physical properties resulting from *quantum confinement* can produce more effective or more efficient catalysts and even entirely new ones. This explains why industry can be expected to show great interest in nanocatalysts.

The *fourth* reason for the interest researchers and technologists are showing in nanoscopic dimensions is that virtually all processes that are important to the lives of humans, plants, and animals operate at nanometre scale. Understanding these processes and the possibility of intervening in them can be extremely valuable in developing new methods to cure diseases. If it becomes possible to target or even influence individual cells (2 micrometres or 2000 nanometres) at the level of specific receptors and processes, it will, for example, be possible to see differences between individual healthy cells and cancer cells. This will improve research into the response to carcinogenic substances and cytostatics, thus leading to the development of more effective therapies. It will probably also allow a reduction in the use of laboratory animals.

2.2 Definitions

Nanoscience and nanotechnology are multidisciplinary areas of science. Nanoscience and nanotechnology are developing so rapidly that researchers have not yet reached consensus on adequate definitions. In explanations and provisional definitions of nanoscience and nanotechnology applied in research and technology programmes, the actual dimensions of the particles studied or processed play a major role.

Physicists, chemists, and biologists – but also information scientists and biotechnologists – are collaborating within varying partnerships on topics whose common feature is that they all involve length scales of from just a few up to approximately 100 nanometres. In physics, chemistry, and biology, definitions are in fact applied on which there is a large measure of agreement. Chemistry deals with the molecules and atoms that make up matter[3]. Physics concerns itself with discovering and formulating the fundamental laws of inanimate nature and using those laws to explain the ways in which matter and energy manifest themselves[4]. Research in biology is scientific research on objects taken from the animate natural world and deals with the origin, construction and function of organisms and the relationship between those organisms and their animate (biotic) and inanimate (abiotic) environment[5]. Dimensions play no role in any of these definitions. Taken together, however, they do give us an impression of the subjects that are relevant to nanoscience and nanotechnology.

A number of descriptions are in fact currently used to clarify what 'nanoscience' and 'nanotechnology' actually mean. Nanotechnology is technology

[3] Foresight Steering Committee (*Overlegcommissie Verkenningen*), Chemie in perspectief (1995).
[4] Foresight Committee on Physics Research (*Verkenningscommissie Natuurkundig Onderzoek*), *Natuurkunde in Nederland: overzicht en vooruitzicht* (1984).
[5] KNAW (1997) Biologie: het leven centraal.

dealing with individual structures with a size of between 100 nanometres and 1 nanometre; nanotechnology is production technology that is precise at molecular level; nanotechnology reveals new properties of matter that are dependent on dimensions and integrates scientific disciplines. Nanoscientific research is the scientific research needed to be able to deploy nanotechnology; physics, chemistry, and biology play an important role in it.

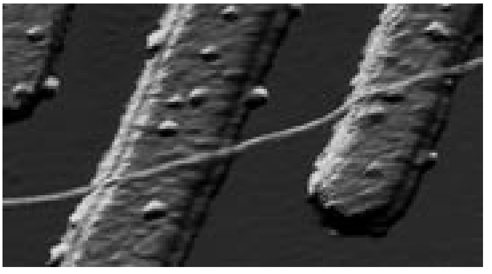


Figure 1. A carbon nanotube stretched between two platinum electrodes on SiO2.[6]

The '*Nanoimpulsprogramma*' financed by the Dutch Ministry of Economic Affairs defines nanotechnology as follows: 'The ability to work at the scale of atoms, molecules, and supramolecular, individually targetable structures (from 1 nm to 100 nm) so as to create complex-functional structures with a fundamentally new molecular organisation. Nanotechnology makes it possible to develop materials and systems whose components and structures display revolutionary new physical, chemical and biological properties, phenomena, and processes associated with their nanodimensions.'

In the United Kingdom, the Royal Society applies the following definition: 'Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale.' Nanotechnology is 'the design, characterisation, production and application of structures, devices and systems by controlling shape and size at nanometre scale.'

In the United States, the National Nanotechnology Initiative does not apply a specific definition but states that nanotechnology 'involves all of the following:
– research and technology development at the atomic, molecular or macromolecular levels, in the length scale of approximately 1-100 nanometre range;
– creating and using structures, devices and systems that have novel properties and functions because of their small and/or intermediate size;
– ability to control or manipulate on the atomic scale.'

[6] S.J. Tans, M. H. Devoret, H. Dai, A. Thess, R.E. Smalley, L.J. Geerligs, and C. Dekker, *Nature* 386, 474 (1997).

In *Small Dimensions and Material Properties*[7], the following definition is proposed: Nanotechnology deals with functional systems and makes use of components with specific properties that are dependent on the dimensions of these separate components or a combination of those components.[8]

In the Netherlands, the Rathenau Institute is currently considering the topic of nanotechnology. By arranging meetings and publications, it contributes to clarifying concepts and revealing the potential of nanotechnology and the dangers that may be associated with it (see appendix). In normal usage, the term 'nanotechnology' is used more frequently than 'nanoscience', but given the current state of research virtually all nanotechnology is in fact still nanoscience. Actual application of knowledge and skills at nanometre scale for production purposes is still only possible to a very restricted extent. Nor will all the nanoscience research that is being carried out lead in the foreseeable future to nanotechnology that can be applied in practice. Nevertheless, we are currently only in the early stages of development and in theory major breakthroughs can be expected in the foreseeable future.

Nano-object	**New properties**	**Applications**
Relocatable atoms on a surface	Ultimate model object for scientific studies in materials science	(indirect)
Biomolecular motors	Model objects for scientific studies in molecular cell biology	(indirect)
C60 fullerenes	High electron affinity	Improved magnetic properties
TiO2 nanoparticles	Monodispersed particles whose colour can be determined	Solar cells, sunscreens
Quantum dots	Colour and electronic properties that can be precisely determined	Dyes, Nanoelectronics and quantum computers
Carbon nanotubes	Good electrical conductor Great mechanical strength	Nanoelectronics and quantum computers, nanosensors, Ultra-strong materials
Polymers/glasses/nanochannels	Miniaturisation of chemical reactions	'Lab on a chip'
Liposomes	Biodegradable compartments	Drug delivery Veterinary use
Photonic materials	Tuneable transmission of light	Telecommunications Optical computers
Nanomagnetic materials	Improved magnetic properties	Data storage

[7] G. Schmid, M. Decker et al. (2003), *Small Dimensions and Material Properties – A Definition of Nanotechnology*, Bad-Neuenahr Ahrwieler, Europäische Akademie.
[8] See *Small Dimensions and Material Properties*, pp. 13-16

Considering the various different definitions or descriptions of nanotechnology currently in use, we find the following common features. ‘Nanoscience’ and ‘nanotechnology’ are collective terms dealing respectively with the science and the technology that take their name from the magnitude at which they work: between 1 and 100 nanometres. Another feature is that matter is manipulated at atomic or molecular level and that at this scale it takes on new properties, or properties become perceptible that are not perceptible at macroscopic scale. The science and technology concerned have consequences for physics, chemistry, and biology and for combinations of these.

3 Nanoscience and nanotechnology: some remarks

3.1 Undesirable effects of nano-objects on human health and the environment

The presence of nanoparticles in the environment is by no means new. Examples include various forms of dust released during mining or certain industrial processes and particles released by motor vehicles during the combustion of diesel fuel. River and marine clay also contain nanosized particles.

Nanoscience and the associated nanotechnology are currently leading to the production of a wide range of different types of particle with dimensions at the nanometre scale. Exposure to these during production, further processing, or application can produce harmful effects on human health and the environment. We already know that some of these new nanoparticles, for example those made up of carbon, can in principle be easily absorbed through the skin or by being breathed in and can cause serious damage. In some cases, moreover, we need to take account of environmental pollution by nanoparticles resulting from their production and/or use, with consequent effects on organisms.

In the case of *quantum dots* consisting of cadmium selenide, toxic substances are released because they are biodegradable. Whether 'buckyballs' (soccer ball shaped carbon structures) are biodegradable is unclear but their average life and distribution give reason for serious concern. A recent report has shown that they can spread unhindered through groundwater and enter the food chain through worms.[9]

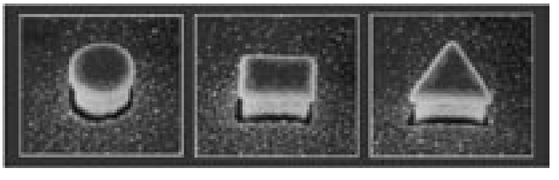


Figure 2. Few-electron quantum dots[10]

Because of their small dimensions, nanoparticles probably have different biological effects to those of macroparticles because they can penetrate cells more easily. The cell membrane is a natural barrier that prevents the contents of the cell leaking out and also prevents the entry of all kinds of foreign, toxic substances. However, cells still need to be able to absorb nutrients and excrete waste products, and there is a wide variety of proteins in the membrane that can transport substances in or out. These substances are recognised due to their size and chemical properties, meaning that the cell is kept free of undesirable compounds.

Some of the nanoparticles now being developed for therapeutic use are of approximately the same dimensions and chemical properties as the fat molecules

[9] G. Brumfiel, A Little Knowledge..., *Nature*, Vol. 424, no. 6946, 17 July 2003, p. 246.
[10] L.P. Kouwenhoven, D.G. Austing, S. Tarucha, Reports on Progress in *Physics* 64 (6), 701-736 (2001).

making up the cell membrane, meaning that they can pass through this barrier. The idea is that once they have entered the cell they will do their work and then be broken down and excreted naturally. If this does not happen, the cell becomes disordered, resulting in its dying or multiplying out of control. Here too, we need to pay careful attention to potential negative side-effects. The necessary research takes a great deal of time and in the case of new types of particles sometimes requires the development of innovative techniques before studies can be carried out properly. Methods of measurement, for example, will probably need to be developed in order to assess the uptake of new types of particles in the body, their dispersal into the different organs, and their possible conversion and excretion. Such techniques are also necessary, *mutatis mutandis*, in order to assess how these particles behave in the environment and whether they are absorbed by nonhuman organisms. It is important for protocols to be kept of such methods and, whenever possible, for them to be validated and harmonised internationally.

Numerous industrial illnesses were and still are the result of exposure to volatile particles. Up to now, the unwanted effects of these particles have been studied using conventional research models as part of inhalation toxicology and epidemiology, for example by means of chronic inhalation studies on laboratory animals. These studies have shown that both the size and surface properties of the particles affect the extent to which they are absorbed in the body and their toxicity. The rate of absorption and toxicity of most particles is greater the smaller they are. However, it is not only the size of the particles that is significant but also the nature of their surface.

A number of recent publications deal with the toxic effects of nanoparticles and their possible absorption in tissue. Some of them investigate the following substances and effects:

– Titanium dioxide and zinc oxide nanoparticles in sunscreens produce free radicals in the skin and damage DNA.[11]
– Experiments show that ultra-fine particles cause a greater infectious reaction in the lungs than larger particles.[12]
– Carbon nanotubes are more toxic in the lungs of mice than quartz dust particles.[13]
– Exposure to hydroxyapatite nanoparticles leads to dose-related inhibition of the growth of human liver cells and induces apoptosis (cell death).[14]
– Ultra-fine particles can pass through the blood-brain barrier via the nasal mucosa, thus entering the brain.[15]
– Carbon nanoparticles (buckyballs) cause brain and DNA damage in fish.[16]

Some people are concerned that developments in nanoscience and nanotechnology will be so rapid that toxicological investigation of possible undesirable effects on human health and the quality of the environment will lag far behind. It is up to government to determine what is permissible, on the basis of generally accepted principles of legislation and regulation.

The health and environmental risks of nanoscience and nanotechnology can be controlled within the framework of existing legislation, for example that relating to health and safety at work, consumer goods, the environment, and medication. This is framework legislation setting out the necessary protection of human health and the environment in general objectives. The regulations regarding specific substances (or agents) are contained in 'orders in council' (*algemene maatregelen van bestuur (AMVBs)*). The ministries of Agriculture, Nature and Food Quality; Social Affairs and Employment; Housing, Spatial Planning and the Environment; and Health, Welfare and Sport regulate the way substances should be dealt with which constitute a danger to human health and to the environment, establishing the standards and conditions with which the information to be provided must comply.

Proper regulation of the introduction of new nanoparticles requires additional provisions in the form of AMVBs. That takes time, for one thing because of the

[11] R. Dunford, A. Salinaro et al. 'Chemical oxidation and dna damage catalysed by inorganic sunscreen ingredients,' *FEBS Letters*, volume 418, no. 1-2, 24 November 1997, pp. 87-90.
[12] G. Oberdörster (2000), Pulmonary effects of inhaled ultrafine particles, *Int. Arch. Occup. Environ. Health*, 74, 1- 8.
[13] C.-W. Lam, John T. James, Richard McCluskey, and Robert L. Hunter (2004), Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal installation, *Toxicol. Sci*, 77, 126-134.
[14] Z.-S. Liu, S.-L. Tang and Z.-L. Ai, (2003), Effects of hydroxyapatite nanoparticles on proliferation and apoptosis of human hepatoma bel-7402 cells, *World J. Gastroenterol*, 9, 1968-1971.
[15] G. Oberdörster, Z. Sharp, V. Atudorei, A. Elder, R. Gelein, W. Kreyling and C. Cox (in press 2004), Translocation of inhaled ultrafine particles to the brain, *Inhalation Toxicology*.
[16] G. Oberdörster, 227th Meeting of the American Chemical Society, 28 March-1 April 2004.

need for European and international harmonisation. To support additional regulatory provisions, more research is necessary on the potential toxic effects of nanoparticles and their kinetics within organisms and the environment. One example of this is the Nanopathology project forming part of the European Commission's Fifth Framework Programme. This project aims to develop diagnostic methods for detecting micro-particles and nanoparticles that are relevant to pathological processes.[17] The results[18] of this and other research, for example in the context of the National Nanotechnology Initiative (NNI) in the United States, will be important in formulating national and international policy.

Some believe that there should be a moratorium on nanoscience and nanotechnology for the present, according to the principle that 'one needs to formulate rules before playing a game'. As yet, not all risks attaching to nanoparticles are known, even though we do already know that some of them have harmful effects and even though we can assume that that is also the case with others. But a moratorium cannot be based on a consideration of benefits and risks, nor is it in proportion to the potential dangers posed by nanoparticles. Imposing a moratorium would ignore the great significance that nanoscience research and the development of nanotechnology have for a wide range of practical applications.

In the words of Dr Renzo Tomellini, head of the European Commission's Unit for Nanosciences and Nanotechnologies (interview[19] June 2003), 'A moratorium would cause us to lose positive momentum, impoverish our knowledge and ability to understand and decide, and waste precious opportunities to develop useful technologies.' However, Dr Tomellini also stated 'We do not wish to originate negative externalities. One cannot, as happened too many times in the past, produce, deliver goods and services, create wealth and provide employment, but pollute, cause environmental disasters and problems to people's health.'

This statement makes clear that a thoughtful and balanced approach is necessary when dealing with nanoscience and nanotechnology.

What we must do is find a solution to the dilemma of either 'doing nothing' or imposing a moratorium. Nanoscience and nanotechnology can continue to develop on condition that researchers and producers make efforts to introduce a painstaking and transparent form of self-regulation. Normal safety considerations must be respected when actually carrying out research. Research institutions and companies that deploy nanotechnology must ensure that proper safety measures are observed. When nanoparticles are used or applied outside the area of research, the legislature must decide whether special measures are needed to protect humans and the environment, doing so on the advice of experts, for example the Health Council of the Netherlands (Gezondheidsraad), the National Institute for Public Health and the Environment (RIVM), and the Food and Consumer Product Safety Authority (VWA). Any ad hoc systems of regulation should be preceded by a survey of current and proposed developments, to be carried

[17] See for example Nanotechnologies: *A Preliminary Risk Analysis on the Basis of a Workshop organized in Brussels on 1-2 March 2004 by the Directorate General Health and Consumer Protection of the European Commission.*

[18] http://europa.eu.int/comm/health/ph_risk/documents/ev_20040301_en.pdf.

[19] 26 June 2003; *Cordis News*.

out by research institutions and industry under the auspices of the appropriate ministries.

3.2 Uncontrolled spread of abiotic self-replicating systems

'Nanobots' are robots at nanometre scale. From the conceptual point of view, they are extrapolated from what can be found in every modern factory, namely programmed machines that carry out a particular task. In his first popular book on nanotechnology, *Engines of Creation*, Eric Drexler[20] extrapolated from such actual robots to the molecular world, suggesting that robots could in principle also exist at molecular scale. The concept of nanobots is based on two principles, firstly that of taking individual atoms and locating them elsewhere using an *atomic force* microscope (AFM) or a scanning tunnelling microscope (STM) and secondly the fact that living systems are full of complex macromolecular machines. Molecular machines would combine atoms and construct larger molecules in the same way as a robot in a car factory carries out welding operations on cars brought to it by the assembly line. Such nanobots could perhaps also be organised using a molecular assembly line.

An example calculation

There is a problem with nanobots, however, namely that of scale. This can be illustrated by means of a simple calculation. Let us assume that a single operation is required to make a single molecule of sucrose by bonding together one molecule of glucose and another of fructose.[21] Let us also assume that it takes one millisecond[22] to carry out that operation. One gram of sucrose consists of 1,000,000,000,000,000,000,000 molecules[23] of sucrose, meaning that the same number of combination operations must be carried out to produce a single gram of sucrose. Using a single nanobot, it will therefore take 1000 billion years to make one gram of sucrose. Producing one gram of sucrose in one day would consequently require 1,000,000,000,000,000 (one million times one billion) nanobots. This gives us food for thought when considering the number of nanobots needed to stock the shelves of our local supermarket with 1 kilogram bags of sugar.

We are used to thinking in terms of the robots used in factories but their complexity is insignificant when we compare them with the tiny 'machines' that nature uses to work on individual molecules. An example of a natural 'machine' that 'holds onto' sucrose is shown in figure 3. Each little ball represents an atom and each line a bond between a pair of atoms. Each machine consists of thousands of atoms. One reason why they are so complex is that the atoms or molecules that they work with are difficult to hold on to because they have a relatively large amount of kinetic energy. They also need to be held on to in the

[20] K.E. Drexler (1986), *Engines of Creation*, Garden City, New York: Anchor Press/Doubleday.

[21] A molecule of sucrose consists of two components: one molecule of glucose and one of fructose.

[22] In biological systems, one millisecond per operation is a normal rate for reactions catalysed by enzymes.

[23] One thousand times one billion times one billion, i.e. 1×10^{21}.

right way if they are to bond with other atoms or molecules. There is therefore good reason for researchers to get excited about the subject of nanobots.

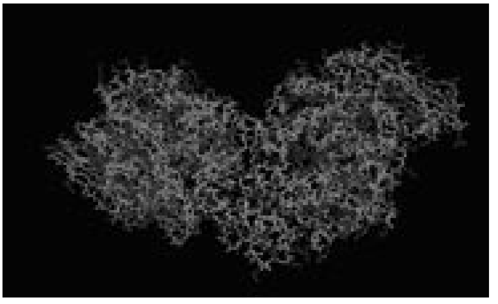


Figure 3. Three-dimensional structure of the enzyme sucrose phosphorylase[24]

Why are nanobots supposed to be dangerous?

Assuming the possibility to build a nanobot, the question arises of how we could produce billions and billions of them. By means of self-replication, was Drexler's answer. He proposed building nanobots that would then build other nanobots for specific purposes such as manufacturing sucrose. However, these would also need to be able to self-replicate because otherwise the large numbers referred to above would need to be made by humans, which is impossible. The danger Drexler foresaw – the 'grey goo' scenario – was that these tiny machines would multiply out of control and spread all over the world. We need to put this in the right perspective.

The first *scanning tunnelling* and *atomic force* microscopes were built twenty years ago. Since then, it has only proved possible in a few isolated cases and under special circumstances to construct or compose only a single individual molecule. A certain amount of knowledge and experience has now been acquired with moving atoms across a surface, for example to construct the letters 'IBM'. It is of course best to avoid saying that something will 'never' happen if there is no solid theoretical basis for doing so. But given what has been done up to now and the complexity of natural nanomachines, it is safe to say that the construction of billions and billions of self-replicating nanobots by human intervention is a highly unlikely scenario. In actual fact, Eric Drexler has since revised his views on this matter.[25]

3.3 Nanoscience and biotechnology

Nanoscience and nanotechnology relate to length scales, units, and dimensions which also occur in nature. The structures of all main biological molecules and systems (proteins, enzymes, DNA and RNA, ribosomes, viruses, etc.) have nano-

[24] D. Sprogoe, L.A.M. van den Broek, O. Mirza, J.S. Kastrup, A.G.J. Voragen, M. Gajhede, L.K. Skov: Crystal Structure of Sucrose Phosphorylase from Bifidobacterium Adolescentis, *Biochemistry* 43 pp. 1156 (2004).

[25] C. Phoenix, K.E. Drexler (2004), Safe exponential manufacturing, in: *Nanotechnology* 15, pp. 869-872.

scale dimensions. This is not entirely a matter of chance. All naturally occurring compounds have been formed over a long period of evolution by means of bottom-up self-assembly and self-replication processes. In recent decades, research in molecular biology and supramolecular chemistry has shown that it is possible to incorporate into particles with measurements at least in the nano-interval the information that is needed to bring about and control complex processes or to acquire special properties of materials (see, for example, the special issue of the journal *Science* in 2002 on supramolecular chemistry and self-assembly[26]).

Biological nanostructures have developed over periods covering billions of years. It can hardly be expected that chemistry and technology will develop so rapidly in the next few years as to make such things as non-biological replication possible in the foreseeable future. There is quite simply too much knowledge lacking. The catalytic systems that are now frequently referred to by chemists as self-replicating are in fact merely autocatalytic systems. Examples include the formation of peptides and DNA fragments from amino acids and nucleotides, respectively, via templates (blueprints) that consist of the products that are to be produced.[27] [28]

These are relatively simple processes that take place under conditions that are precisely determined. However, it is a feature of life processes that they are extremely complex, involve a great deal of feedback, and take place under a wide variety of circumstances. Designing and constructing self-replicating nanobots must therefore be considered extremely unlikely even at some point in the future, and probably technically impossible, at least from the point of view of the application of bottom-up self-assembly processes.

It is not inconceivable, though, that nanochemists cooperating with molecular biologists will soon take an entirely different approach, for example by using semi-finished natural products to produce functional and perhaps self-replicating nanosystems. This may involve such things as the use of viruses and genetically modified cells, thus linking up with biotechnology. This is an area that is still at the frontiers of knowledge, but it is expected to become increasingly important in the next few decades.

Biotechnologists and nanotechnologists are already collaborating to develop materials with special properties. David A. Tirrell's research group at the California Institute of Technology, for example, uses genetically modified cells to produce proteins that fold in a totally controlled manner, thus creating nanostructured materials with special hydrogel properties.[29] At the Scripps Institute, also in the United States, research is being carried out on genetic modification of virus particles so that these 'bio-nanosystems' can act as a template for bonding

[26] *Science*, special issue on Supramolecular Chemistry and Self-Assembly, Vol. 295 (no. 5564), 2002, 2313-2556.

[27] Including work by R. Ghadiri of the Scripps Institute in the United States; see A. Saghatelian, Yokobayashi, Y., Soltani, K., & Ghadiri, MR (2001), A chiroselective peptide replicator. *Nature* 409, 797-801

[28] A. Luther, R. Brandsch, G. von Kiedrowski (1998), Surface-promoted replication and exponential amplification of dna analogues, *Nature* 396, 245-248.

[29] D. Tirrell, W.A. Petka, J. L. Harden, K.P. McGrath and D. Wirtz (1998), Reversible Hydrogels from Self-Assembling Artificial Proteins, *Science* 281, 389.

particles of gold and crystallising cadmium sulphide in order to create nanoballs and nanothreads with special properties.[30] Some people have a negative image of bio-nanotechnology because they think it can lead to the copying of life itself. From a historical perspective, this is understandable because in the past various other new technologies were considered – certainly by laymen – to involve imitating life itself. The clock is one example, as are the steam engine and the computer and, more recently, artificial intelligence and biotechnology. Repeatedly, it was in fact awe and incomprehension that produced that impression, rather than any realistic reason.

3.4 Practical and ethical aspects

Nanoscience is in part an incremental continuation of 'ordinairy' science in the fields of chemistry, physics, and biology. There is also no essential difference between the resulting technology and existing technology. To some extent, however, there are also new developments that lead to the production of new types of particles and products. Spectacular applications of nanotechnology are anticipated that may have major consequences for our everyday lives. Given the possible effects of 'new style' nanotechnology on society, the researchers and technologists that promote these developments have an ethical duty as scientists to inform the public – realistically and in good time – of what is possible and of the consequences for society in the short and long term. It is then up to society as a whole to determine to what extent the positive options should be made use of and how far the associated uncertainties can be accepted.

The Rathenau Institute for technology assessment is currently looking into nanotechnology. By arranging meetings and publications, it contributes to clarifying concepts and revealing the potential of nanotechnology and the dangers that may be associated with it (see appendix). A recent report by the Institute argues in favour of clearly structuring of responsibility regarding both the opportunities and the threats associated with nanotechnology.[31] In this connection, the Institute publishes a newsletter intended to foster open discussion of nanoscience by scientists, government bodies, business and industry, and the general public.

Up to now, assessment and decision-making regarding the introduction of new technologies and, for example, new substances have primarily been a matter for scientists and politicians. Figure 4 gives a diagram of the main outlines of this process. The first phase involves scientific assessment of the potential risks of new technologies or new applications of chemicals, for example drugs and pesticides/herbicides. The second phase, that of risk management, is intended to determine rules for application or use so as to minimise the risks. Finally, the public is presented – more or less – with a *fait accompli*.

[30] See for example C. Mao et al. (2004), Virus-Based Toolkit for the Directed Synthesis of Magnetic and Semiconducting Nanowires, *Science* 303, 213-217.

[31] Rathenau Institute: Report on Workshop on Opportunities and Threats associated with Nanoparticles (17 February 2004).

Figure 4. The basic principles of the risk analysis process as applied internationally by the FAO, WHO, and EU.

Greater public involvement in the decision-making process is also considered desirable in wider circles. However it has seldom been possible up to now – either in the Netherlands or elsewhere – to effectively bring about public participation in decision-making on scientific issues. The confused ideas the public have regarding genetically modified organisms (GMOs) are a direct result of the inept way in which the public were informed about the introduction of this new technology. The work of the Terlouw Committee was well meant, but it commenced too late and consequently had insufficient influence on public opinion. This greatly restricted the possibility of carefully developing policy aimed at the safe and profitable application of GMOs.

It may perhaps be possible to proceed more effectively as regards the introduction of nanotechnology. Doing so will require steps to be taken as soon as possible to keep the public informed about the scientific and technical developments. In addition, representatives of the public should be involved in substantive discussion of the pros and cons of nanoscience and nanotechnology.

Some years ago, as part of the discussion of GMOs, a group of European researchers considered the question of how consumer involvement and confidence could be strengthened and of how account could be taken, at an early stage in the decision-making process, of the response and wishes of the public.

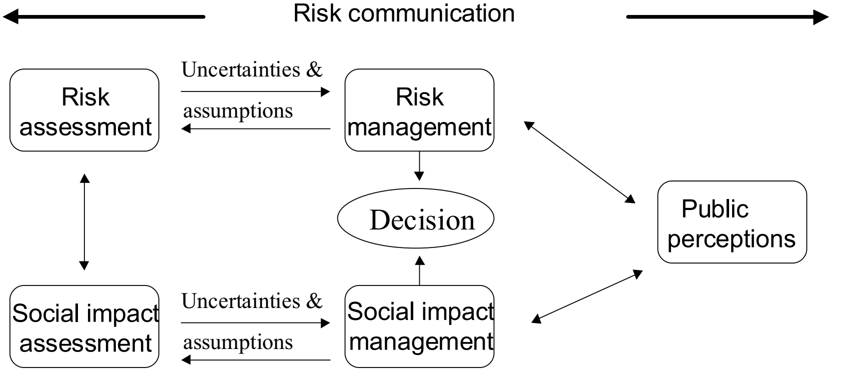


Figure 5. Model of integrated scientific and public risk analysis. (Based on D. Barling, H. de Vriend, J.A. Cornelese, B. Ekstrand, E.F.F. Hecker, J. Howlett, J. H. Jensen, T. Lang, S. Mayer, K.B. Staer and R. Top (1999). The social aspects of food biotechnology: a European view, *Environ. Toxicol. Pharmacol.*, 7, 85-93.)

Figure 5 shows how the decision-making process could be structured according to Barling et al. (1999). In this model, scientific development and public discussion go hand-in-hand and the public are informed at each stage of the process and involved, where possible, in evaluation and decision-making.

The model also requires *risk manageme*nt and *social impact management* to include consideration of the application of two important principles, namely those of precaution and proportionality. The precautionary principle means that new technologies should not be applied if they appear to involve risks to health or the environment, even if those risks have not been established beyond doubt by scientific research. The proportionality principle requires that every chosen measure should be both necessary and suitable in the light of the goals that have been set. This therefore means that when analysing the potential risks of proposed applications, we need to consider both the costs and the benefits.

To advance scientific research in general and to develop useful applications, it is important that research can be carried out. Effective provision of information about that research can contribute to the results being accepted. In this connection, it should be remembered that providing information about new technology does not automatically lead to its being accepted; confidence in new developments and proper understanding of it are two different things.

Organising an approach such as that set out in figure 5 requires thorough preparation. The provision of information in the national press and the organisation of a number of parliamentary and public hearings are just some components of effective public management of the introduction of new technologies, in this case nanotechnology. Government will need to play a central role; that too is a responsibility within the context of the ethics of science. Such discussion will need to involve all the stakeholders concerned, namely government, business and industry, consumer and environmental organisations, and various sections of the public. It is also important for discussion to be entirely open, in direct confrontation with panels of experts. Presentations on the achievements of nanoscience and nanotechnology, followed by debate, can make an important contribution to creating a broad basis of support, certainly if they are broadcast on television.

4 Conclusions and recommendations

On the basis of the above considerations, the following conclusions and recommendations can be formulated regarding the development of nanoscience and nanotechnology.

1 **Conclusion**

Research and technology at nanometre scale represent important developments for science and technology. They constitute an incentive for both science and the knowledge-based economy. Nanoscience and nanotechnology contribute greatly to developments in ICT and health care.

Recommendation

The government should provide ongoing political support for nanotechnology and nanoscience. A good start has been made by the recent application-oriented initiatives within the framework of 'BSIK', the Decree Regarding Subsidies for Investment in the Knowledge Infrastructure (Besluit Subsidies Investeringen Kennisinfrastructuur). However, targeted support should also be provided for fundamental scientific research, for example via the Netherlands Organisation for Scientific Research (NWO).

2 **Conclusion**

All health and environmental aspects of research and technology at nanometre scale are covered by existing legislation, but more specific legislation still must be introduced. The greatest public danger posed by nanotechnology is in the uncontrolled use of nanoparticles and the unrestrained distribution of nanoparticles which are not biodegradable, or which do break down but in doing so produce toxic degradation products. From the perspective of proportionality, imposing a moratorium on nanoscience and nanotechnology would be entirely undesirable, given that it would lead to unacceptably tight restrictions on Dutch research and the generation of knowledge with a view to practical applications.

Recommendation

The Ministry of Education, Culture and Science should promote that new and existing research in nanoscience can be continued. Research institutions should ensure that they have adequate safety precautions in place, similar to those applying to the use of chemicals: research proposals should be assessed carefully in the light of the effects they may have on health and the environment. The government should draw up new legislation within the existing legal frameworks.

3 **Conclusion**

The health and environmental risks of nanoscience and nanotechnology can be controlled by means of existing legislation, such as that relating to health and safety at work, consumer goods, the environment, and medication. Proper regulation of the general introduction of new nanoparticles necessitates additional legislation in the form of 'orders of council' (Algemene Maatregelen van Bestuur (AMVBS). This requires more research on potential toxic properties of nanoparticles and their kinetics within organisms and the environment. It may be necessary to develop new toxicity models. Coordination with international developments, particularly in the European Union, is essential both for policy development and research.

Recommendation

– The Ministry of Education, Culture and Science and the Netherlands Organisation for Scientific Research (NWO) should promote research on the possible toxicity of nanoparticles.
– The Ministry of Education, Culture and Science should ensure that if research into the toxicity of nanoparticles entails the needs for to more detailed regulation, any regulatory proposals should be coordinated with the European Union.

4 **Conclusion**

It is a major concern that suitable and reliable public information should be provided on what is or is not possible in the fields of nanoscience and nanotechnology. As with biotechnology and genetic modification, there is no realistic cause for concern regarding nanotechnology. However, providing information may be insufficient to ensure public confidence. There is as yet only a restricted amount of public discussion. The Rathenau Institute is developing initiatives aimed at focusing attention on the implications of nanotechnology.

Recommendation

The Ministry of Education, Culture and Science and the Ministry of Economic Affairs should promote the provision of public information regarding nanoscience and nanotechnology. It is crucial for the public to be actively involved in discussion of the future of this scientific research and of application of its results.

5 **Conclusion**

Evaluating the risks associated with nanoparticles requires analysis of the risks posed by these particles and of the influence of products containing nanoparticles on our daily lives. Communication regarding evaluation should involve government, business and industry, researchers, consumer and environmental organisations, and politicians. Such evaluation should commence as soon as possible.

Recommendation

It is up to the Government to initiate a properly structured, open discussion of the value of nanoscience and nanotechnology and of any potential risks. The Ministry of Education, Culture and Science and the Ministry of Economic Affairs should encourage participation in this discussion, bearing in mind the lessons to be learned from the introduction of genetically modified crops.

6 **Conclusion**

Constructing structures by mechanical or industrial means with molecular precision is a complex and time-consuming process; it has nowhere near achieved the level of efficiency and effectiveness with which such structures are created in animate nature. It is highly unlikely and unrealistic from a practical point of view to assume that it will ever become possible to construct molecular machines (‘nanobots’).

Appendices

Appendix 1 Remit and composition of Study Group on the Consequences of Nanotechnology

In a letter (OWB/DIR/03/202627) dated 8 August 2004, the Minister of Education, Culture and Science requested the Academy 'to draw up a report surveying, on the basis of the scientific literature, the potential dangers and problems, including those which must be considered highly speculative, and then critically analysing them and determining how realistic they are.'

The Academy Board decided to set up a study group with the remit of drawing up such a report. The members of the study group are:

Prof. J.H. Koeman	emeritus professor of toxicology, Wageningen University and Research Centre, chair of the Academy's Science and Ethics Advisory Committee; *chair*
Prof. C. Dekker	professor of molecular biophysics, Delft University of Technology
Prof. R.J.M. Nolte	professor of organic chemistry, Radboud University Nijmegen
Prof. D.N. Reinhoudt	professor of supramolecular chemistry and technology, University of Twente
Prof. A. Rip	professor of the philosophy of science and technology, University of Twente
Prof. G. T. Robillard	professor of membrane enzymology, University of Groningen
J.D. Schiereck	policy officer, KNAW Bureau

Appendix 2 Letter of 8 August 2003 from the Minister of Education, Culture and Science

Education, Culture and Science

Ministry of Education,
Culture and Science

Europaweg 4
P.O. Box 25000
2700 LZ Zoetermeer
T: (079) 323 23 23
F: (079) 323 23 20

To the President of the KNAW
Prof. W.J.M. Levelt
P.O. Box 19121
1000 GC Amsterdam

Your letter of	Our ref.	Contact	Zoetermeer
	OWB/DIR/03/20627		8 August 2003
Subject	Enclosure(s)	Direct dialling	
Nanotechnology		2288	

Dear Prof. Levelt,

The Dutch government and the public knowledge infrastructure are putting an increasing volume of funds into research in nanotechnology. Nanotechnology is a priority in the context of ICES-KIS (Interdepartmental Committee for Economic Structure Enhancement/Knowledge Infrastructure Working Party); considerable attention can also be expected to be devoted to nanotechnology in the framework of the activities of the innovation platform. In this respect, the Netherlands is following international trends. In the United States and the United Kingdom, for example, a large amount of funding has gone into nanotechnology in the past few years and it is also being given an increasingly prominent position in EU research programmes.

At the same time, a certain amount of public concern is growing in the UK and the US regarding dangers that may be associated with nanotechnology. That concern has to do, for example, with the uncontrolled proliferation of self-replicating nanomechanisms and biological applications. Even though these and other dangers would seem at present to be rather speculative, it is nevertheless advisable for us to take this matter seriously and to apply the precautionary principle in an appropriate manner. That is the only way in which we can ensure a broad basis of public support for further research in this field. In this context, we can learn from what has happened in the area of genetically modified organisms.

With these considerations in mind, the UK government requested the Royal Society and the Royal Academy of Engineering to investigate the ethical and societal implications of nanotechnology. In the United States, the House and Senate are currently looking at proposals for investigating and otherwise considering the problems that may be associated with the development of nanotechnology.

Now that the Netherlands is also increasingly prioritising research in nanotechnology, I believe that we should follow the example of the UK and the US and consider the possible ethical and social issues in this field. As an initial step, I wish to request the Academy to draw up a report for me, surveying, on the basis of the scientific literature, the potential dangers and problems, including those which must be considered highly speculative, and then critically analysing them and determining how realistic they are. In the light of that report, I shall then consider whether it is necessary to take further steps, for example by requesting the Rathenau Institute to produce materials as a basis for promoting public debate on this matter.

Yours sincerely,

The Minister of Education, Culture and Science,
(Maria J.A. van der Hoeven)

Appendix 3 Letter of 29 September 2004 from the KNAW to the Minister of Education, Culture and Science regarding the report Nanoscience and nanotechnologies: opportunities and uncertainties published by the Royal Society and the Royal Academy of Engineering, United Kingdom

Royal Netherlands Academy of Arts and Sciences

Visitors' address:
Het Trippenhuis
Kloveniersburgwal 29

Correspondence address:
PO Box 19121
1000 GC Amsterdam

T (020) 551 0700
F (020) 620 4941

To the Minister of Education, Culture and Science,
Ms M.J.A. van der Hoeven
PO Box 16375
2500 BJ The Hague

Our ref. DIR/JSc/7405
Direct dialling. (020) 5510 734/728
E-mail: jan.schiereck@bureau.knaw.nl
Subject British report on consequences of nanotechnology

Amsterdam, 29 september 2004

Dear Ms Van der Hoeven,

In August 2004, the Royal Netherlands Academy of Arts and Sciences (KNAW) submitted a report to you entitled *How big can small actually be? Some remarks on research at the nanometre scale and the potential consequences of nanotechnology.* In July 2004, the Royal Society (RS) and the Royal Academy of Engineering (RAE) in the United Kingdom published the results of a study of the consequences of nanoscience and nanotechnology entitled *Nanoscience and nanotechnologies: opportunities and uncertainties.* When *How big can small actually be?* was published, the KNAW held out the prospect of providing you with additional comments on the RS/RAE report; this letter contains those comments.

From the point of view of actual substance, the objectives of the KNAW and RS/RAE projects were similar, namely to provide answers to such questions as: what are nanoscience and nanotechnology; what potential effects – both positive and negative – can they be expected to have; and what are their societal and ethical implications? Although the approaches taken by the RS/RAE and the KNAW differed, the two reports in fact came to virtually identical conclusions.

With the exception of metrology, the KNAW memorandum deals with almost all the issues considered in the RS/RAE report. Given its length, the British report provides more details and examples; a number of these – concerning societal and ethical implications – deserve to be mentioned as a supplement to the KNAW memorandum.

Metrology

Metrology at nanometre scale is vital to developments in scientific research and technology. What is particularly important is the ability to measure lengths and forces at nanoscale with great accuracy but at the same time in a simple manner. Given that there is as yet no standardised system of measurements, steps should be taken to ensure that methods of measurement are uniform and compatible. The RS/RAE advised the British government to take urgent action in this area. This issue is also important as regards developments in nanoscience in the Netherlands. Consideration should be given to collaborating on metrology with researchers and policymakers in the United Kingdom so as to make it possible to keep close track of developments from an early stage and also to take action to influence matters. One can also expect the importance of this issue to be felt at EU level. Consideration should be given to whether it would be in the interest of nanotechnology in the Netherlands to make preparations for a campaign at EU level (in collaboration with the United Kingdom).

Ethical and social aspects

It is important that the positive effects of nanotechnology should ultimately benefit all levels of society. The KNAW wishes to note the risk of a "nano-gap" arising between those who are in a position to profit from the advantages of nanotechnology and those who are not.

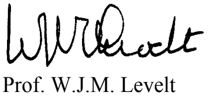
One should be cautious about making commitments regarding the potential benefits of nanotechnology in the medical field unless there is clear and demonstrable evidence (a principle that naturally applies to all new developments in medical technology). In the short and medium term, improvements or reinforcement of human sensory faculties can only be expected in sight and hearing. In the view of the KNAW and the RS, such developments should be made available to all levels of society if there is a medical indication. Medical practitioners and researchers display a clear and well developed concern for ethical issues. One should expect that they will be very much alert to any undesirable ethical implications of the use of nanotechnology.

Nanotechnology may prove beneficial in reducing carbon dioxide emissions; quickly and cheaply identifying pathogens; purifying water; providing cheap raw materials; and producing components for electronic circuits. The report mentions applications in the field of sensors ("pervasive sensing"), information systems, and communication technology that may also have military ramifications. It is not possible to make a clear distinction between military and civil developments but one cannot exclude the possibility that nanotechnology may lead to a new arms race. The application of nanotechnology in a military context may have a negative effect on public acceptance of nanoscience and nanotechnology.

In the short term, most of the ethical consequences are likely to involve research and technology that affect privacy and civil liberties. In the longer term, technology aimed at increasing human capabilities may also have ethical consequences. In this context, the combination of nanotechnology, biotechnology, ICT, and cognitive sciences will play a major role.

Some of the potential effects of nanotechnology are extremely far-reaching, going well beyond those of the more basic sciences that contribute to nanotechnology. Like the KNAW, the Royal Society and the Royal Academy of Engineering are in favour of a much more prominent place being given to studying these consequences and to public discussion when developing nanotechnology than is normally the case when a new technology is being developed.

The Board of the Royal Netherlands Academy of Arts and Sciences



Prof. W.J.M. Levelt
President

Appendix 4 Sources of information

A great deal has been published on nanoscience and nanotechnology, and on the associated possibilities and risks. Sources include:

Arnall, A.H. (2003), *Future Technologies*, *Today's choices*, London: Greenpeace Environmental Trust.

Colvin, Vicky L. (2003), The potential environmental impact of engineered nanomaterials, in: *Nature Biotechnology*, 21, 166-1170.

Dekker, C. (2003), *Nanotechnologie, fascinatie voor het kleine* (foundation day address). Delft, Delft University of Technology.

Drexler, K.E. & R.E. Smalley (2003), Nanotechnology: Drexler and Smalley make the case for and against 'molecular assemblers', in: C*hemical and Engineering News*, December 1.

Dyson, F.J. (2003), The Future Needs Us!, in: *The New York Review of Books* Vol. 50: 2.

ETC Group (2003), *The Big Down*, Winnipeg.

ETC Group (2003), *The Little BANG Theory*, Winnipeg.

Europäische Akademie (2003), *Small Dimensions and Material Properties – A Definition of Nanotechnology* (Graue Reihe, no. 35).

European Commission (2004), *Towards a European strategy for nanotechnology* (Commission Communication (2004) 338 def.), Brussels.

Feynman, R.P. (1960), There's Plenty of Room at the Bottom, in: *Engineering and Science* Vol. 23:5.

Joy, B. (2000), Why the future doesn't need us, in: *Wired* Issue 8.04.

National Science and Technology Council (2000), *National Nanotechnology Initiative: The Initiative and its Implementation Plan*.

Phoenix, C., K.E. Drexler (2004), Safe exponential manufacturing, in: *Nanotechnology* 15, pp. 869-872.

Rathenau Institute (2004), Verslaglegging Workshop Kansen en Risico's van Nanodeeltjes.

Rathenau Institute (2004), *Om het kleine te waarderen... Een schets van nanotechnologie: publiek debat, toepassingsgebieden en maatschappelijke aandachtspunten* (working document 93).

Reinhoudt, D.N. (1999), *Nanotechnologie; uitdagingen en realiteit van de ondergrens* (foundation day address). Enschede: University of Twente.

Roco, M.C., W.S. Bainbridge (Eds.) (2001), *Societal Implications of nanoscience and nanotechnology*. Dordrecht: Kluwer.

Royal Society and Royal Academy of Engineering (2004), *Nanoscience and nanotechnologies: opportunities and uncertainties*, London.

Schmid, G., M. Decker et al. (2003), *Small Dimensions and Material Properties – A Definition of Nanotechnology*, Bad-Neuenahr Ahrwieler: Europäische Akademie.

Smalley, R.E. (2001), Of Chemistry, Love and Nanobots, in: S*cientific American* 285, pp. 76-77.

www.nanoned.nl
www.cordis.lu/nanotechnology
www.nano.gov
www.nanotec.org.uk
www.rathenau.nl