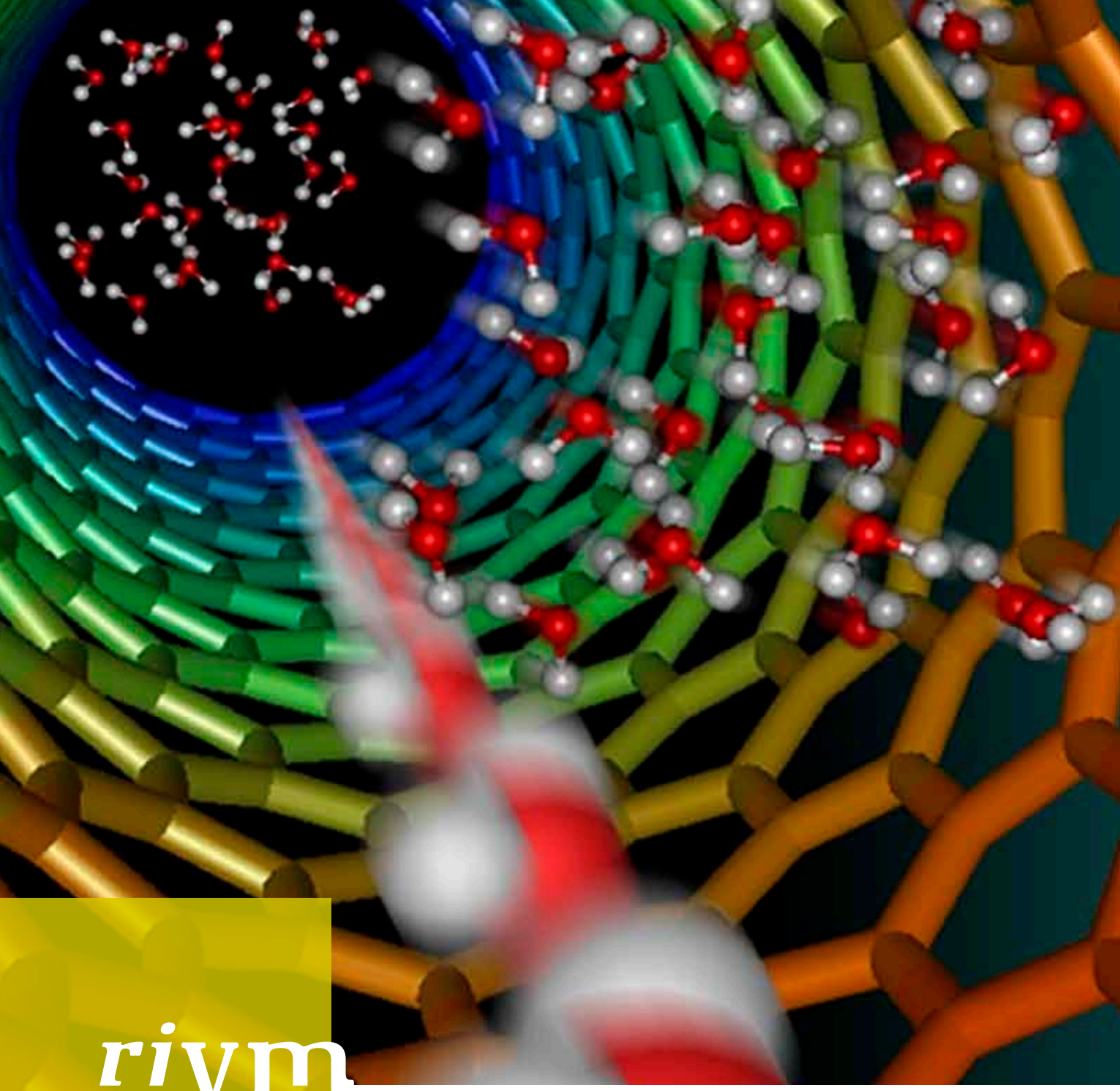

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National Institute
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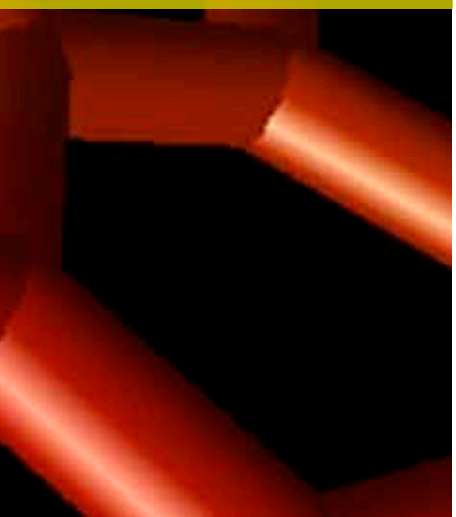
and the Environment

Report 601785004/2009

M. van Zijverden | A.J.A.M. Sips (ed.)

Nanotechnology in perspective: summary

Risks to man and the environment



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RIVM Report 601785004/2009

Nanotechnology in perspective: summary

Risks to man and the environment

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This study was carried out on behalf of the Netherlands Ministries of Housing, Spatial Planning and the Environment (VROM); Health, Welfare and Sport (VWS) and Social Affairs and Employment (SZW), by the Risks of Nanotechnology Knowledge and Information Centre (KIR nano).

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This report is a translation of the report 'Nanotechnologie in perspectief: samenvatting. Risico's voor mens en milieu' (RIVM report 601785001 that was published in 2008.

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Foreword

This is a summary of the report ‘Nanotechnology in perspective’ which provides insight into the risks posed by nanotechnology to humans and the environment. The complete report (no. 601785003) can be found on the RIVM website (www.rivm.nl).

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Abstract

Nanotechnology in perspective
Risks to man and the environment

The Risks of Nanotechnology Knowledge and Information Centre (KIR nano), a Dutch government-supported observation organisation based at RIVM, has provided an overview of the potential risks to both man and the environment of exposure to nanoparticles. The focus is on free, non-degradable and insoluble nanoparticles found in medical applications, food, consumer products and the environment.

Scientific data compiled to date demonstrate that adverse effects due to exposure to nanoparticles cannot be ruled out. However, much more information is required to be able to estimate the risks of nanoparticles equally as well as those of other non-nano chemicals. Nevertheless, hundreds of products containing nanomaterials are currently available commercially, a situation which clearly necessitates investigation of the exposure and toxicity of these materials in the near future. Unfortunately, the research questions to be answered are so numerous that it will take years to compile the relevant data.

KIR nano recommends that research be focused primarily on those questions that provide information critical to the assessment of risks to man and the environment. Depending on the perspective – worker, consumer, patient, or the environment – the starting points can then be defined for controlling or limiting the risks. Information generated in the strictly regulated world of medical applications (e.g., on methodology) could constitute a valuable asset in other areas of research and application, where the data and dossier requirements are not as exacting.

Key concepts in the coming years include expanding our knowledge of nanoparticles and making this knowledge readily available to avoid duplication of research; identifying and where necessary taking appropriate risk management measures, deciding on which areas of research the Netherlands wishes to contribute to this field, supporting research & development and promoting cooperation between government bodies and agencies, the scientific community and trade and industry.

Key words:
nanotechnology, risks, health, environment, consumer products, medical applications, food, worker safety

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Rapport in het kort

Nanotechnologie in perspectief
Risico's voor mens en milieu

Het Kennis- en Informatiepunt Risico's van Nanotechnologie (KIR nano) van het RIVM heeft de potentiële risico's van blootstelling van gefabriceerde, vrije, onafbreekbare en onoplosbare nanodeeltjes in kaart gebracht. In dit rapport worden de risico's voor de mens als werknemer, patiënt en consument behandeld, evenals risico's voor het milieu. Drie toepassingsgebieden zijn daarbij relevant: geneesmiddelen en medische technologie, voedselproductie en consumentenproducten.

De huidige stand van zaken van de wetenschap laat zien dat risico's niet uit te sluiten zijn. Er ontbreekt echter nog veel kennis om de risico's even goed in te kunnen schatten als voor 'chemische stoffen niet in nanovorm'. Toch zijn er al vele honderden producten waarin nanomaterialen zijn verwerkt op de markt. Dit vereist op korte termijn veel onderzoek naar de blootstelling en toxiciteit van deze materialen. Helaas is het aantal onderzoeksvragen dusdanig groot en fundamenteel van aard dat het nog jaren zal duren voordat alle informatie is vergaard.

KIR nano adviseert daarom het onderzoek vooral te richten op die vragen die cruciale informatie voor de risicobeoordeling voor mens en milieu bieden. Afhankelijk van het perspectief van werknemer, consument, patiënt of milieu zijn oplossingsrichtingen gedefinieerd voor het beheersen van de risico's. Informatie die in de streng gereguleerde wereld van medische toepassingen wordt gegenereerd kan met name vanuit methodologisch oogpunt zeer waardevol zijn voor andere toepassingsgebieden, waar de dossiervereisten en dus veelal ook de informatievergaring (veel) beperkter voor zijn.

Kernbegrippen voor de komende jaren zijn samen te vatten onder KOKOS: *K*ennis vergroten en uitwisselen om dubbeling van onderzoek te voorkomen, *O*plossingsrichtingen en risicomanagement, *K*euzes maken in bijdragen vanuit Nederland aan dit onderzoeksveld, *O*nderzoek & Ontwikkeling, en *S*amenwerking bevorderen tussen wet- en regelgevende kaders, wetenschap en bedrijfsleven.

Trefwoorden:
nanotechnologie, risico's, gezondheid, milieu, consumentenproducten, medische toepassingen, voeding, arbeidsveiligheid

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1 Introduction

This document provides a comprehensive summary of the preliminary notification report 'Nanotechnology in perspective' by the Risks of Nanotechnology Knowledge and Information point (KIR nano). (For the full text see RIVM report 601785003). The purpose of this preliminary report is to outline the current state-of-affairs and the main developments in the field of nanotechnology and make an initial analysis of the potential risks to man and the environment. The report concentrates on three areas in which nanotechnology is applied: medical applications, foodstuffs and non-food consumer products. The potential risks posed by nanotechnology to the environment and in terms of the health and safety of workers are also specifically considered.

1.1 What is nanotechnology?

Nanotechnology is the entirety of new, emerging technologies which uses substances or structures on a nanoscale. Nanoscale refers to a feature characterised by dimensions in the order of 100 nanometres (nm) or less. For comparison: that is 80,000 times smaller than the cross-section of a human hair. The diameter of a single atom is in the order of 0.1 nm.

At these dimensions chemical substances sometimes acquire new, different properties and they offer new possible applications. For example, nanomaterials may have special mechanical, optical, electrical and magnetic properties which the same substances do not have at greater dimensions. These same properties could also pose risks to man and the environment.

Although there are as yet no officially recognized definitions, nanotechnology has provisionally been defined by the International Organization for Standardization (ISO) as follows (ISO draft business plan, 2007):

- *Understanding and control of matter and processes at the nanoscale, typically, but not exclusively, below 100 nanometres in one or more dimensions where the onset of size-dependent phenomena usually enables novel applications*;
- *Utilizing the properties of nanoscale materials that differ from the properties of individual atoms, molecules, and bulk matter, to create improved materials, devices, and systems that exploit these new properties.*

Working definitions of other nanotechnology-related terms have been drawn up by the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) of the European Commission, and these definitions have also been used in this report.

1.2 What does nanotechnology have to offer the ordinary (Dutch) citizen?

Nanotechnology is used to change the properties of products. In this way products can be made stronger, more elastic, scratch-resistant or much smaller. Applications can be found in medicines and medical aids, foods and consumer products, the environment and in energy technology. These applications can improve the quality of life and the environment and can also lead to more sustainable products. For example, nanotechnologies can significantly improve the quality and efficiency of healthcare, increase the efficiency and sustainability of food production and lead to substantial energy savings.

People can already come into contact with nanotechnology applications in many areas. There are, for example, hundreds of consumer products with nanotechnologies on the market which contain real nanomaterial. In particular nano forms of silver, titanium, cerium and carbon nanotubes are used in these products. Examples include nanoparticles of titanium oxide and zinc oxide as UV reflectors in sun barrier creams, carbon nanotubes used as material strengthening in car tyres and natural clay particles in car bumpers. Nano coatings are used on spectacles, scratch-resistant sensors and self-cleaning windows. Nanocrystals make cutting and drilling equipment extra hard and durable. Furthermore there are products on the market which make surfaces water and dirt-resistant. Packaging for foodstuff and textiles too, are given an anti-microbial treatment through the application of a thin layer of nanoparticles. Nanotechnologies are also used to make clothing crease-resistant and dirt-resistant or, through nano-electronics, to add functions to medical applications. Nanotechnology enables electronics to be made ever smaller, faster and more multi-functional. This makes it possible to incorporate ‘intelligence’ into ever more products. Ultimately, nano, bio and IT technologies will become more and more closely integrated.

By far the most potential applications of nanotechnology are currently still in the research and development phase and are expected to appear on the market over the coming years.

1.3 What does nanotechnology represent for the Netherlands’ knowledge economy?

In the Netherlands and elsewhere people have high expectations with regard to the economic potential offered by nanotechnology and its benefits to society. In the document entitled ‘Kabinetsvisie nanotechnologieën - van klein naar groots’ [The Dutch government’s vision on nanotechnologies - from small to great] (Netherlands’ government, 2006) the Netherlands’ government sets out its vision on nanotechnologies. In that document the view is expressed that nanotechnologies could become a ‘major driver’ of our knowledge economy and society. It is forecast that the worldwide sales of products containing nanotechnologies will grow from € 25 billion in 2004 to € 450 billion in 2010.

The Netherlands has a number of internationally leading academic research groups and companies both in the area of developing nanotechnologies and in the area of risks. This knowledge combination could make an important contribution to economic growth.

At present there are four generations of nanotechnologies:
First generation: nanostructures with passive, fixed structures and functions. These include chemical substances with particles on a nanoscale which are often applied as part of or as an ingredient in types of products which already exist.
Second generation: active nanostructures which further to a stimulus can exhibit a change in properties, such as size, form or conductivity. For example, nanoparticles which target pharmaceuticals at a tumour in the body and under the influence of a radiation source release the pharmaceutical in the tumour.
Third generation: networks of nanosystems: three dimensional networks, bio and chemical assembly techniques and robotics on a nanoscale.
Fourth generation: molecular nanosystems which can be designed per particle, e.g., for advanced genetic therapies. Self-assembling structures on a nanoscale also come under this fourth generation.

Right from the first generation, new products have been developed which bring together various fields of application. Because of the new functionalities, these products could fall between the various legislative provisions. Such observations have already been made in the field of pharmaceuticals and medical technology, but they are also quite conceivable in other domains. In 'Van klein naar groots' the government has set out a vision for the first and second generation.

The third and fourth generations of nanotechnologies are related to the synthetic biology which brings together Nanotechnology, Biotechnology, Information Technology and Cognitive science (NBIC). On 28 January 2008 the Synthetic Biology Committee was set up by the Royal Netherlands Academy of Arts and Sciences (KNAW), the Health Council of the Netherlands and the Advisory Council on Health Research. This committee will look at the situation in the Netherlands, developments in the field and the opportunities for synthetic biology. It would be advisable for this committee to look at the possible risks associated with these nanotechnologies even at this stage.

1.4 What are the potential risks?

At the same time signals are coming from the scientific community that the application of these technologies could pose certain risks for consumers, workers and the environment. These are mainly applications that actually contain nanomaterial which could be released at a certain stage in the life cycle of that particular product. These risks are, however, more difficult to determine than those of chemical substances which are not in a nano form and are therefore, to some extent, still largely unknown. In line with the report 'Betekenis van nanotechnologieën voor de gezondheid' [Health significance of nanotechnologies] published by the Health Council of the Netherlands (April 2006), in the document setting out its vision 'Kabinetsvisie nanotechnologieën: van klein naar groots' [The

Dutch government's vision on nanotechnologies - from small to great] (Netherlands' government, 2006], the Dutch government stated that these risks should be addressed with caution, care and common sense. The basic premise of the Netherlands policy on managing the risks is therefore the current substances policy in force and the risk policy as formulated in the VROM policy document 'Nuchter omgaan met risico's' [Coping rationally with risks] (VROM, 2004).

1.5 Risks of Nanotechnology Knowledge and Information Centre (KIR nano)

As indicated, there are currently numerous nanotechnology products on the market, although the risks to man and the environment are generally still difficult to estimate. In such a situation it is very important to identify the potential risks and gather as much relevant information as possible. On behalf of the Netherlands Ministries of Housing, Spatial Planning and the Environment (VROM); Health, Welfare and Sport (VWS) and Social Affairs and Employment (SZW), the Risks of Nanotechnology Knowledge and Information Centre (KIR nano) was set up at the National Institute for Public Health and the Environment (RIVM). KIR nano reports to these ministries.

The tasks of the KIR nano are:

- **to identify** scientific advances in the area of nanotechnology and relevant information about the risks to man and the environment. To do this KIR nano needs to be part of national and international networks (e.g., through EU projects such as the European Observatory and NanoImpactNet) and keep abreast of developments in the areas of research, policy, innovation and applications, et cetera;
- **to advise** the government on matters concerning the assessment of risks to man and the environment, e.g., in the context of REACH (the European legislation on chemical substances);
- **to take part** in scientific fora, including in the areas of standardization and risk research (SCENIHR, ISO) and play a coordinated role in fora which develop methodologies for the risk assessment of nanotechnology (i.e., estimating the risks to man or the environment, including the associated uncertainties further to exposure to a substance), such as OESO (Organisation for Economic Co-operation and Development);
- **to inform** government authorities and professionals about the risks of nanotechnology by providing independent and reliable information (e.g., on www.rivm.nl/rvs), and contribute to the dialogue with industry and society at large.

1.6 Scope

The observations made in this report could offer starting points for policy on how to deal with the risks associated with nanotechnologies. However, the following should also be noted:

- Initial research has shown that following uptake the body has great difficulty eliminating *purposely manufactured , free, non-degradable and insoluble nanoparticles*. This report therefore concentrates on the potential risk posed by such particles. Particles which are unintentionally released (as fine dust) and particles which occur naturally (volcanic dust) will be left aside. This report will mainly consider the risks of nanoparticles (of three dimensions smaller than 100 nm), but where this involves not just nanoparticles, the broader term of nanomaterial (with at least one dimension smaller than 100 nm) will be used;
- It lies beyond the scope of this report to make recommendations, but starting points for policy concerning the risks of nanotechnologies are identified;
- This report deals with the toxicological and ecotoxicological risks of exposure to *first generation nanomaterials* which the population and the environment could already be exposed to *at the moment*. This is the case for *medical applications, foodstuffs* and *consumer products*;
- The following target groups have been identified: workers, (this includes research workers and production workers, as well as those professionally involved in the application of nanomaterials), patients, consumers, the general population and the environment;
- The report provides a snapshot of the present moment in time. Rapid developments are taking place in both applications and risk research. Therefore parts of the report will eventually be overtaken by events. The picture outlined will be updated in future reports;
- This report provides an overview of the potential risks of nanotechnologies by combining two factors: the degree to which man and the environment are exposed to nanomaterials, and the toxicity of such nanomaterials. The combination of these two factors determines the ultimate risk. Societal factors, such as risk perception and differences in the acceptance of risks, fall outside the immediate scope of this report.

2 Nanotechnology: what are the risks?

This report is mainly concerned with synthesized, free, non-soluble and non-degradable nanoparticles because it is generally expected that these particles pose the most threat of risk to human health and the environment. There are indeed indications that some of these nanoparticles can behave in the human body in the same way as fine dust and asbestos.
Humans and the environment are already exposed to nanoparticles as a result of incineration or volcanic and erosion processes. Knowledge about exposure to such particles and their effects on man and the environment is relevant to be able to estimate the risks of exposure to a nanomaterial after it has been inhaled. As yet, it appears that contamination with nanomaterials through other exposure routes (such as via the skin and the gastrointestinal tract) is only possible to a limited extent.

Under the general system for the assessment of risks, the risk of a substance is determined by the hazard posed by the substance itself times the degree to which a person is exposed to that substance. This results in the following formula:

RISK = EXPOSURE x TOXICITY

A certain dose of a substance will result in harmful effects (toxicity). To be able to establish these effects, an organism must thus first actually be exposed to such a dose.

This formula applies to nanomaterials too: the ultimate risk is determined by the toxicity of a specific nanomaterial to a human, plant or animal and by the exposure to the substance in question. A specific nanomaterial may be toxic, but if the degree of exposure is small, the ultimate risk will also be small. The toxicity is determined by a number of factors, such as a nanoparticle's ability to pass through certain barriers in humans, plants or animals and find its way into tissues and organs where it can then have damaging effects.
The actual exposure is also dependent on various factors, such as the surroundings or the structure in which the nanomaterial occurs (e.g., bonded or as 'free' particles), the degree to which contact with the material is possible, et cetera.

It is also important to always bear in mind the target group for which the risks need to be estimated (tailored approach).

2.1 Why is it difficult to establish the risks of nanomaterials?

As stated, the free nanoparticles increase the chance of human and environmental exposure. When nanoparticles are bonded in a hard coating, for example, the chance that a person or the environment will be exposed is fairly small. However, when such products are subject to wear and during waste

processing nanoparticles can still be released and, as a result, humans and the environment will be directly exposed. When the particles are further insoluble and non-degradable, they can also accumulate in organisms or humans and be damaging.

The research required is very extensive and complex. The reasons for this include:

- The risks posed by a nanoparticle cannot simply be derived from the risk profile of substances in non-nano form or that of other nanoparticles. Apart from the chemical composition, characteristics such as form, surface and size are also important;
- A chemical substance may have a great many different sizes and forms of nanoparticles, each with their own unique properties and specific risks. For the time being, the risks need to be separately determined for each form of a nanomaterial;
- For chemical substances not in nano form there is often a *body of knowledge* on which to fall back on. Based on the physico-chemical properties of substances the behaviour and toxicity of a substance with similar properties can to some extent be predicted. This *body of knowledge* is not yet available for nanomaterials (including nanoparticles);
- Ideally, for toxicological research the complete series of tests (including animal testing) would have to be carried out for every nanoparticle (i.e., for every particle size and form, et cetera.). This is because it is not yet clear what criteria are essential to be able to characterize nanoparticles and set the dosage. Such research is now only taking place for highly specific applications (e.g., pharmaceuticals) and for national and international research programmes;
- Apart from the ethical and financial drawbacks of such extensive toxicological research, it is to a certain extent unclear whether the normal testing methods can be applied to nanoparticles.

In short, nanomaterials add a new dimension to toxicological and ecotoxicological research and its interpretation. It is important that priority is given to establishing what properties of nanomaterials result in toxicological or ecotoxicological effects. Only then can a suitable dose descriptor be defined which provides a correct description of the relationship between dose and toxicological or ecotoxicological effects. The risks to man and the environment are set out in the sections below.

2.2 Dosimetry

The usual way in which the dosage of a chemical substance is described, by weight (e.g., gram active chemical substance per kg dry matter), does not appear to be a good measure to describe the effects of nanoparticles. This is because various physico-chemical properties have to be taken into account. These include: elementary composition, density, crystalline structure, solubility, charge, polarity, conductivity, melting point, hardness, optical and magnetic properties, dimension, morphology, particle size and particle size distribution, surface area and composition of the surface layer (e.g., coating, charge).

It is still unknown which of the above properties are important in determining the behaviour, toxicology and ecotoxicology of nanoparticles. As stated above, a proper dose descriptor is vital to be

able to interpret toxicological and ecotoxicological research and to derive threshold limit values for exposure. Until that time, in all studies it is recommended to gather as much information as possible on the above characteristics for the administered dose.

2.3 The human risks

Exposure
Exposure refers to the amount of substance to which humans are exposed. Exposure consists of two separate steps:

1. external exposure: this is the dose (amount of nanomaterial) which people can come into contact per time unit;
2. internal exposure: the dose (amount of nanomaterial) which is actually taken up by the body and which can reach the tissues and organs.

Here too, the issue of relevant dosimetry is important, reinforced by the lack of suitable measuring equipment or measuring methods.

Depending on the application, humans may be exposed through various routes:

- via the airways (inhalation);
- via the skin;
- via the gastro-intestinal tract (orally);
- through injection or from implants (parenteral exposure).

In the area of fine dust a lot of research has been done on exposure via the airways. With the arrival of nanotechnology, more attention is now given to exposure to particles via other routes.
Exposure can occur in the workplace, through the consumption of food and drinking water, through the use of consumer products such as creams, and by the ingestion and administering of medical applications based on nanotechnology. In addition, contact with nanomaterials is possible from the environment through contact with soil, surface water or air.

Kinetics
Kinetics is how substances behave in the body. The most important concepts in kinetics are often summarised with the acronym ADME (Absorption, Distribution, Metabolism and Excretion). These terms refer to the uptake, distribution, metabolism and elimination of a substance by the human body.

The need to gain insight into the behaviour of nanomaterials in the human body is widely recognized. Research has shown that:

- certain particles can reach the body via the airways. The properties which are critical for uptake are not yet known;
- uptake via the intact skin has not been proven. For products such as sun barrier creams there is an ongoing debate about whether the nanomaterials used in these products can enter the body

through skin which is burned or through ‘flexing skin’ (moving areas such as wrists and knee hollows);
- whether there is uptake through the gastro-intestinal tract is still largely unknown. Here too, it is not known which particle characteristics are critical to absorption across the gut wall;
- to be able to assess the risks of nanoparticles it is vital to know whether or not the nanoparticles of a substance can actually pass through the initial barriers of the body (airways, skin, gastro-intestinal tract). If that is the case, then full toxicological research must be carried out. If the nanomaterial degrades to the conventional chemical substance before uptake, existing toxicological data could possibly be used. After passing the initial barrier, nanomaterials can move into tissues and organs and possible toxicological effects may occur;
- it appears that smaller nanoparticles are distributed to more organs than larger ones. However, the precise relationship between particle properties, such as size, and distribution within the body is still unknown;
- a number of studies have focused on the question of whether nanoparticles can pass through natural barriers such as the placenta or the blood/brain barrier. This information is of vital importance to be able to estimate toxicological effects. There are indications that a number of types of nanoparticles can reach the brain but whether they actually pass through the barrier still has to be verified. Research on transplacental transport is still limited but is beginning to gain more attention;
- the metabolism plays no great part in the kinetics of free, insoluble nanomaterials;
- partly because of this, the body has difficulty in eliminating nanoparticles as a result of which they can accumulate in the body.

Toxicokinetic research on nanomaterials requires reliable measuring methods of which there are, unfortunately, none as yet. In particular, there is a lack of methods which can demonstrate the presence of nanoparticles in tissues and organs. These methods are essential to be able to show that exposure to nanomaterials also leads to the uptake of nanomaterials by the body. Furthermore, it is not yet possible to extrapolate the results from one particle size to another, for example. This implies that toxicokinetic (in vivo) research, including a detailed characterisation of the nanoparticle dosage, must be carried out for each type of particle. From the literature it unfortunately appears that doses are often poorly documented. This also makes it almost impossible to compare study results.

Toxicology

For the time being, standard toxicological research would appear to be useful for soluble nanoparticles. The specialist field of particle toxicology has still largely to be developed for insoluble and non-degradable nanomaterials. However, experience drawn from fine and ultra-fine dust research could also be used for this. Although ultra-fine dust comprises particles which have not been deliberately produced (e.g., as a combustion product of diesel), the knowledge gained in this area is highly relevant for research on the risks related to deliberately produced nanoparticles.

Experiments in test animals have shown that long-term exposure to fine and ultra-fine dust can lead to increased concentrations in the brain. Studies with volunteers have also shown that ultra-fine particles can contribute to cardiovascular diseases, such as athlerosclerosis, thrombosis and contraction of the blood vessels. They furthermore have an impact on brain function. Various animal studies suggest that nanoparticles have similar effects as fine and ultra-fine dust further to exposure by inhalation.

The body of knowledge on the toxicity of inhaled nanoparticles is rapidly growing. Owing to the limited availability of properly characterised nanoparticles, few studies in organisms (in vivo) have been conducted. Most publications are therefore concerned with the effects on isolated cells, and it is difficult to interpret these results in terms of effects on a whole organism. In the mechanism of toxic effects it would appear that the formation of potentially damaging molecules (oxidative stress) and inflammatory factors play a crucial role. These effects include inflammation and the formation of tumours in various organs, for example. Poland et al. (2008), for example, showed that in rodents injected with carbon nanotubes, inflammation occurs which is characteristic of the early stages of mesothelioma (asbestos cancer). These nanotubes are specially manufactured to meet the established 'asbestos criteria' (length to diameter ratio, strength and non-degradability).
Less is known about the toxicity of nanoparticles further to long-term exposure and the harmful effects from other exposure routes.

Risks
It is still insufficiently clear what the toxicity of nanomaterials is, and to what degree people are exposed to nanomaterials. The latter because there is currently no overview of products which include nanomaterials, and in what form they exist in those products. Once that information is available, an initial estimate of exposure can be made. If nanoparticles are released from these products then, in principle, people can be exposed to free nanoparticles.

Recent findings with carbon nanotubes indicate that exposure to these tubes can result in risks. However, it must be emphasized that the study results should be seen as an indication of possible effects for this type of carbon nanotubes with these particular characteristics. These effects therefore cannot simply be applied to other types of carbon nanotubes and particles with different physico-chemical properties.

2.4 Risks to the environment

Due to the presence of nanotechnology in a great many products, emissions to the environment may be expected to increase, which may have an impact on ecosystems. For an analysis of the risks of nanoparticles for the environmental compartments of water, air, soil and sediment, please see the full report (no. 601785003).

Emission, fate and behaviour, and exposure
The greatest emission of nanomaterials may be expected to occur during the use and waste processing

of products. It is unknown at this time, however, to what extent purposely manufactured nanomaterials are present in natural ecosystems.

It is furthermore not yet really possible to uniformly characterise nanoparticles released into the environment. Little is also known about the fate and behaviour of the particles once they end up in the environment. Knowledge about the behaviour of aerosols (solutions of small particles in a gas) can be drawn on for the air compartment while colloid chemistry may offer a possible starting point for the water compartment. In both cases, however, there is still an insufficient basis available to be able to properly describe the fate and behaviour of nanoparticles. This makes the search for suitable testing systems complicated and hinders the extrapolation of results from test systems to the environment itself.

Ecotoxicology and indirect effects on man and the environment

Ecotoxicology covers many different plant and animal species. A great deal of research is necessary before observed effects can be extrapolated to higher organisms such as mammals. There are indications that nanoparticles in the environment may have undesirable anti-microbial effects. However, it is impossible to say at this time what risks posed by nanoparticles are relevant and possibly of concern for organisms in the ecosystem. Both direct and indirect effects may be possible. Indirect effects are, for example, the ability of nanoparticles to bind with substances. In this way nanoparticles could remove environmentally-polluting substances from water, for example. But in the same way nanoparticles could perhaps remove nutrients or cause a high concentration of contaminating substances in sediments because of the nanoparticles which bind with them and are then deposited. Finally, nanoparticles in the environment can reach humans. Potential routes for this include the consumption of drinking water, agricultural produce and farm livestock.

Risks

There is still no widely accepted estimation method or a valid theory with which to establish the risk of nanoparticles in the environment. Research is currently beginning which will look at establishing and quantifying the determinants which influence the risks of nanoparticles (such as particle size distribution and the specific nature of the surface of the nanoparticles).

3 Nanotechnology: identifying the blank spots

There are still a great many gaps in the knowledge necessary to be able to estimate the risks of exposure to nanomaterials for humans and the environment at a comparable level to that for chemical substances which are not in nano form. These gaps relate to populations which come into contact with nanotechnology (workers, consumers, patients and the environment) and areas of applications (agrofood, consumer products, medical applications and sustainable environmental applications) on the one hand and the lack of suitable research methods, on the other. In general, the risks relating to medical applications have been best defined. Due to the nature and controlled use of the products, the level of exposure is set. Legislation requires that possible toxic effects are constantly evaluated, although it is important to check whether this evaluation is complete. Other areas, however, hardly benefit from the methodological and other knowledge which research on medical applications provides, while the same type of particles are being used (e.g., nano silver). There is also too little collaboration between product developers and risk researchers to ensure that products are developed on a safe basis. The same applies to the evaluation of knowledge about changing material properties on a nanoscale in the light of potential risks.

3.1 Lack of information on exposure

When we look more closely at what knowledge is missing, what first becomes apparent is that there is no clear overview of the degree to which nanomaterials are used. Most attention is devoted to possible exposure of employees working professionally with nanomaterials. It is, however, insufficiently clear to what extent consumers and the environment are exposed to nanomaterials. The lack of adequately validated and accepted methods to be able to measure and characterise nanomaterials properly plays a significant part in this. This means that it cannot be reliably determined what workers are exposed to in the workplace, for example. It can also barely be determined whether nanomaterials can already be found in the environment, the human body or in food, for example.

Although in employment situations it is possible to adopt ‘good practices’, such as wearing suitable protective clothing. However there are knowledge gaps with regard to the effectiveness of such measures. For the environment and the consumer, however, there are hardly any starting points for protective measures when dealing with products containing nanomaterials.

3.2 Lack of information on possible toxicity

Apart from the lack of information on exposure there is also a lack of information about the possible toxicity of nanomaterials to humans and the environment (risk = exposure x toxicity). This makes it

impossible to carry out a quantitative risk assessment. Such an assessment is necessary to substantiate threshold limit values and to estimate the risks to humans and the environment when these threshold values are exceeded. The information which is lacking is of a basic nature. For example, it is still unclear what measure best describes a dose of nanomaterials. For chemical substances not in nano form a dose based on weight (e.g., gram) has been defined. For nanomaterials, however, this would not appear to be a good measure for determining the relationship between dose and effects. This lack of a proper dose descriptor therefore constitutes an important hiatus with regard to both determining and exceeding threshold levels.

The lack of data on actual exposure to and the toxicity of nanomaterials also stands in the way of a qualitative or relative risk estimate (such as a rough classification of nanomaterials in various hazard groups).

3.3 Environmental risks difficult to estimate

Due to the rapid rise of nanotechnology, research on its environmental risks is still in its infancy. This means that even a basic estimate of these risks cannot be made. Given that nanoparticles are being used in ever greater numbers of applications, it is expected that emissions to the environment will increase. It is therefore urgently necessary to examine the entire life cycle of products (from manufacture to the waste stage). However, adequate information for this purpose is lacking in many areas (production, emissions, what particles are found in what products, how waste is disposed of, et cetera). And once nanoparticles end up in the environment, even less is known about their fate and behaviour. This makes it difficult to set up suitable testing systems to measure possible effects on ecosystems.

As the European Commission also concluded, the present legislative framework provides a sound basis to ensure the safety of man and the environment further to exposure to nanomaterials. However, there are some gaps in its application, in the area of enforcement, for example. Nanotechnology is often classified under converging technologies where, together with biotechnology, information technology and cognitive sciences (NBIC), it will lead to new applications. This convergence could mean that applications end up slipping between the regulations and legislative frameworks. As has already been noted for medical applications, it is not always clear whether a product should be viewed as a pharmaceutical or as a medical aid.

4 Conclusions

The phrase ‘risks of nanotechnology to man and the environment’ covers a very broad spectrum of research. It is important to bear in mind that there is no such thing as *the* risks of nanotechnology. The risks depend on the type of nanomaterial (form, size, et cetera), the application method and exposure, and the area of application, et cetera. Therefore we must speak of the acknowledged and potential risks of certain types of nanomaterials in specific situations and applications.

Research and debate on the actual and potential risks posed by nanotechnology to humans and the environment currently focus only on first generation nanomaterials; this report too. Here the concern, quite rightly, is with manufactured, free, non-degradable and insoluble nanoparticles. A great deal still remains unknown about the risks posed by these particles. To learn more about this, a good starting point would appear to be the way in which chemical substances in non-nano form are assessed.
Key considerations for the coming years should be:

- Increasing and exchanging information and knowledge
- Identifying solution areas and risk management
- Making decisions
- Research & Development
- Cooperation

4.1 Increasing and exchanging knowledge

At present a great deal of international attention is focused on drawing up research agendas. It is also very important to set up and maintain infrastructures to promote the exchange of knowledge and information between stakeholders, application domains and different scientific disciplines.

General concepts about the relationship between particle characteristics and their uptake in the body, for example, are for the time being still difficult to derive. This is because it is expected that relatively little research data will be generated in the coming years for each area of application. It is therefore necessary to integrate knowledge and experience from different application areas to be able to arrive at such concepts in the mid-term (five to ten years) at least. Knowledge about medical applications is relatively thorough and thus, from a methodological viewpoint in particular, offers a good starting point for other areas of application.

The development of safe applications can be promoted by considering the risk assessment and risk management aspects during the development phase. For this researchers developing nanotechnology products can learn from researchers studying the toxicology of free, insoluble particles - and vice versa. Because not only is knowledge and information lacking, but there is also a failure to exchange it. The worldwide consensus is that the above problem requires interdisciplinary cooperation and coordination to prevent the duplication of research. The Netherlands subscribes to this conclusion set out in the

Dutch government's vision on nanotechnology (Netherlands' government, 2006). At present research on risks is insufficiently well organised within the Netherlands, partly because no umbrella activities have been set up for this by the government authorities.

4.2 Identifying solution areas and risk management

A general analysis across the target groups and applications suggests a number of directions in which solutions may be sought to minimise these risks to humans and the environment. *Employees and those professionally* involved in the *application of nanoparticles* can apply the principles of 'good practice'. Some urgency in the development of such practices is therefore required. For *patients* the existing strict admission requirements for medicines must be regularly evaluated in relation to their topicality. There are fewer opportunities available for ensuring that *consumers* are exposed as little as possible to nanomaterials in foodstuffs and consumer products. Tightening up of the legislation and providing information to consumers would appear to be the best options for this. The background to these suggestions is given in Appendix 6 to RIVM report 601785003.

For *the environment* the most obvious place to start is by limiting emissions. Nanoparticles are being used in ever greater quantities, in ever more applications. It is to be expected that, parallel to these developments, emissions to the environment will increase and thus also their effects on ecosystems. Research on the behaviour of nanomaterials in and their possible impacts on the environment therefore also needs to be considered.

4.3 Making decisions

A great deal of basic information is still lacking to be able to arrive at proper quantitative risk estimates. The research questions are numerous and methodological in nature. Good national and international coordination of research can help to fill these knowledge gaps. It would be desirable for a vision to be developed on the basis of which the Netherlands can contribute to risk research. National and international government authorities must set priorities for this.

4.4 Research & Development

Both innovative and applied research for product development will be necessary to be able to determine the most suitable testing methods.

Research on risks should, in the first instance, be directed towards research which will make a significant contribution to a reliable risk assessment. From this perspective it is important to first demonstrate that nanomaterials are actually taken up by the body or are present in environmental compartments in that form. If that is the case, then full toxicological research must be carried out. If the

nanomaterial degrades to the conventional chemical substance before uptake or before it is emitted to the environment, existing toxicological data could possibly be used.

It is recommended that risk research in the area of nanotechnology be conducted on a more pro-active basis in future, particularly with a view to the risks posed by following generations of nanotechnologies. This requires a switch from reactive to anticipatory risk research.

4.5 Cooperation

In estimating the risks of nanotechnology there are three main groups of actors involved, i.e., the legislative bodies, the scientific community, and trade and industry. These three groups need to be aware of each others' questions. In this way a set of priorities can be created in terms of the activities required to fill the knowledge gaps as quickly and efficiently as possible and therefore reduce risks as quickly as possible through risk management.

The linking of research on nano applications and their risks in various domains also offers prospects: the unique properties of nanoparticles which are interesting for applications may also be relevant in establishing risks. What may be seen as an opportunity in one domain (e.g., pharmaceutical drugs which can pass the blood/brain barrier) may in another domain be seen more as a risk (e.g., nanoparticles in the brain). Only cooperation between these domains will lead to progress in society.

Given the advantages which nanotechnologies could bring to society, it would be to the benefit of the various stakeholders to subscribe to the same principle: *the implementation of nanotechnologies in society deserves to succeed, provided that the safety of man and the environment can be guaranteed.*

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