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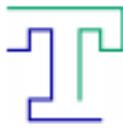
Overview of completed and ongoing activities in the field:

Safety and Risks of Nanotechnology

Authors:

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Karl Höhener



This report has been written by TEMAS AG with kind support of the Swiss Commission for Technology and Innovation (CTI).

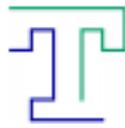
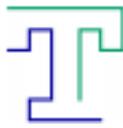
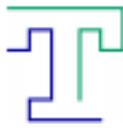


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1 Objectives

The present survey intends to provide a non-exhaustive overview of worldwide studies, completed and on-going, dealing with safety and risk assessment issues of the rapidly developing field of nanotechnology. The focus of the current report is on the following subject areas of nanotechnology:

- Nanoparticles, Nanotubes and Fullerenes
- Medical Applications of Nanotechnologies

Safety assessment of novel drugs and drug formulations (drug delivery) based on nanotechnology, will be taken care of by the current approval process of the US Food and Drug Administration (FDA).

Nanotechnologies bare a high potential for the development of new materials, products and processes with improved performance or even altogether novel properties. At the same time, as with all new technologies, the impact of nanotechnologies on human health, environment and generally on society is up to now most speculative.

Potentially harmful effects of nanotechnology might arise as a result of:

- Nature of the nanoparticles themselves (i.e. chemical reactivity).
- Characteristics of the products made with nanoparticles.
- Aspects of manufacturing processes.

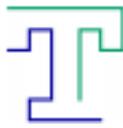
In addition, the fact that new materials, generated through the use of nanotechnological methods, are increasingly used for industrial processes as well as for consumer goods, makes the safety and risk question of nanotechnology even more pressing.

1.1 Definitions

Nanoparticle:

There are probably as many different definitions for nanoparticles as there are different types of nanoparticles. For the scope of this overview nanoparticles are defined through the following characteristics:

- Size: < 100 nm in diameter in their non- aggregated appearance
- Novel properties: novel physical, chemical, biological characteristics as compared to micro-scale particles of the same material or the same bulk material due to their nano-scale dimensions
- Shape: different possible shapes as long as one dimension is < 100 nm, including the following
 - spherical with core
 - spherical without core (nanocontainer, fullerenes)
 - cylindrical (single wall and multiple wall nanotubes)
 - non-spherical (e.g. "nanoplates" with different shapes)



- **Synthesis:** only particles that were synthesized or engineered on purpose. As opposed to Ultrafine Particles (UFPs) which form accidentally as by-products of intended processes (e.g. combustion, mining)

It is widely accepted that there are three major topics which need to be taken into account for the assessment of potential risks of nanotechnology.

1.2 Impact on the environment

To assess the impact of nanoparticles on the environment, information needs to be acquired on the following subjects:

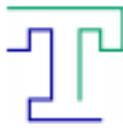
- Release of nanoparticles into the environment.
- Distribution of nanoparticles within the environment (water streams, soil, air).
- Preferential accumulation of nanoparticles (sink).
- Persistence/degradation of nanoparticles in the environment.

1.3 Impact on human health

Similarly, to evaluate the potential effects of nanoparticles on human health or more generally on living organisms (i.e. food chain), it is important to gather sound knowledge on:

- How nanoparticles are absorbed by the human body (skin, lung, gastro-intestinal tract).
- How nanoparticles are distributed within the organism (blood and lymphatic systems).
- In which organs nanoparticles preferentially accumulate (e.g. brain, kidney, liver).
- How nanoparticles are metabolized and eliminated from living organisms.

Furthermore, the promised advantages of nanotechnology are that the properties including chemical reactivity of materials at the nanoscale can change dramatically. On the other hand, the increased reactivity of nanoparticles poses a fundamental problem in view of the voluntary or involuntary release of such particles into the environment with their subsequent uptake by living organisms.



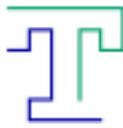
1.4 Ethical, legal and societal implications

It is widely assumed that society can derive major benefits from nanotechnology, but at the same time the societal impact can not be predicted at this point in time and should not be underestimated. Especially the consequences of nanotechnology in conjunction with information-, bio- or medical technologies are difficult to foresee.

In any case, assessment of risks related to self-replicating nano-robots, as described for example in Michael Crichton's book "Prey", belong to the realm of Science Fiction and are not considered in this survey. However, the impact of fiction like "Prey" on the public perception of nanoscience and nanotechnology should not be ignored, especially in view of the announced launch of a movie version of the "Prey" story whose expected release date is not yet known, but assumed to be scheduled for summer 2004.

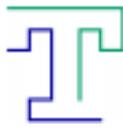
Clearly, the public perception of nanotechnology is a crucial determinant for its successful establishment as a future driving force in the economies worldwide. However, biotechnology, especially its commercial applications within European agriculture and food industries, is a recent prominent example of how the implementation of a new technology can be hampered by public acceptance. Thus, this report presents also publications assessing ethical, political, legal and social implications of nanotechnology.

Last but not least, a further goal of this overview is to identify leading scientists and other opinion leaders active in the above mentioned fields of assessing potential environmental and societal impacts of nanotechnology.



2 Approach

- As a first step, the current status of the debate about the safety of nanotechnology is summarized in chapter 3.1.
- A collection of recent key publications from both, proponents and critics of nanotechnology are summarized in more detail in Chapter 3.2. However, a literature search for publications investigating the toxicology of new synthetic nanoparticles in animals, revealed very few such studies, which indicates that the knowledge of the effects of new synthetic nanomaterials on living systems is still quite scarce. Nevertheless, there is a large body of literature and studies investigating the effects of ultrafine particles (e.g. Diesel exhaust, coal dust, quartz dust) on human health. Since the surface characteristics of ultrafine particles play an important role in their toxicity, it remains to be seen to what extent this knowledge is applicable to the assessment of the potential biological impacts of engineered nanoparticles.
- Current international (EU, USA) programs supporting research on health and environmental safety aspects of the use of emerging nanotechnology products are summarized.
- Key players in the field of risk assessment of nanotechnology are listed (chapter 4).



3 Results

3.1 Summary

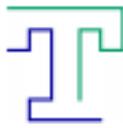
Two recent publications, one commissioned by the Non Governmental Organisation (NGO) Greenpeace and the second one published by the ETC Group (Action Group on Erosion, Technology and Concentration), a Canada-based NGO, take the lead in publicly raising questions about safety of nanotechnology and its future impact on the environment, health and society in general.

Whereas the report initiated by Greenpeace remains quite neutral in terms of policy recommendations, the ETC report proposes that governments should declare an immediate moratorium on commercial production of nanomaterials. In addition the ETC authors suggest the launch of a transparent global process for evaluating the socio-economic, health, and environmental implications of the technology. This ETC report on "Atomtech" provoked a vast echo in the international press and has started the public debate about the future of applied nanotechnology.

On the other hand, consciousness is mounting on the side of the advocates of nanotechnology that scientific studies investigating the effect of nanomaterials on living matter are urgently needed.

For example, Vicki Colvin, Director of the Center for Biological and Environmental Nanotechnology (CBEN) of Rice University, USA, has published a comprehensive review summarizing the current knowledge of the toxicology of synthetic nanomaterials (see 3.2.2.1). This review could serve as a reasonable benchmark for further investigations regarding the toxicology aspects of engineered nanomaterials.

The limited data available on the toxicology of nanomaterials is not surprising, since for example in the United States only a small fraction of nanotechnology and nanoscience funding is devoted to investigating nanotechnology's potential environmental impacts. However, this situation seems to change rapidly. In Fiscal Year 2002, the U.S. National Science Foundation alone awarded ca. \$23 million for educational and societal impact studies and ca. \$30 million for research evaluating environmental and health aspects of nanotechnology. In 2003 the "NANOSAFE" project was funded within the Fifth Framework Programme of the European Union. NANOSAFE assesses risks involved in the production, handling and use of nanoparticles in industrial processes and products, as well as in consumer products. Further calls for such risk assessment projects are planned within the Sixth Framework Programme of the European Union. In addition, in July 2003 the U.S. Environmental Protection Agency invited research applications for the evaluation of potential impacts of manufactured nanomaterials on human health and the environment. Thus, over the last year several studies have been started with the aim to generate hard data that address the physiological effects of nanomaterials. Such studies will be the basis for future exposure recommendations.



3.2 Key Publications on Risk Assessment of Nanotechnology

3.2.1 Non-Governmental Organizations

3.2.1.1 Report of the ETC Group

Title: The Big Down: Atomtech - Technologies Converging at the Nano-scale.

Author: ETC Group (Action Group on Erosion, Technology and Concentration; formerly known as RAFI)

Address: 478 River Avenue, Suite 200
Winnipeg, Manitoba R3L 0C8
Canada

Tel: 001 204 453 5259

Fax: 001 204 284 7871

Email: etc@etcgroup.org

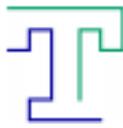
Web: www.etcgroup.org

Date: January 2003

Source: <http://www.etcgroup.org/search.asp?theme=11>

Summary:

This report analysis the scientific, technological, political, ethical, and societal aspects of nanotechnology in detail and concludes by conveying a rejecting standpoint towards all further developments of nanotechnology including research. Note that part of the literature on occupational and environmental particle research from 1980 to this date was not considered for this report. Importantly, policy recommendations are put forward proposing an immediate moratorium on commercial production of new nanomaterials.



3.2.1.2 Report for the Greenpeace Environmental Trust

Title: Future Technologies, Today's Choices; Nanotechnology, Artificial Intelligence and Robotics; A technical, political and institutional map of emerging technologies.

Author: Alexander Huw Arnall

Address: Department of Environmental Science and Technology
Environmental Policy and Management Group
Faculty of Life Sciences
Imperial College London
University of London
Fourth Floor, RSM Building
Prince Consort Road
London
SW7 2BP

Tel.: 0044 (0)20 7594 9340

Fax: 0044 (0)20 7594 9334

Email: alexander.arnall@imperial.ac.uk

Date: July 2003

Source: <http://www.greenpeace.org.uk/MultimediaFiles/Live/FullReport/5886.pdf>

Summary:

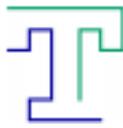
Basic background information on nanotechnology with the following structure:

- Section 1: Introduction (pp 12-13)
- Section 2: Status of research and Development (pp 14-18)
- Section 3: Applications and Markets:

Already introduced products and those due for introduction in short and medium-term. (pp 21 - 31)

- Section 4: Reality versus Vision (hype) (pp 32 - 35)
- Section 5: Potential environmental and social risks (pp 35 - 40)
- Section 6: Summary (41)

Overall, a concise, comprehensive, multifactorial and rather unbiased, although commissioned by Greenpeace, view of the state of the art of nanotechnology and its current and future applications. The report differentiates between risk aspects of nanotechnology's present-day and future products, as well as between main socio-economical and environmental concerns.



3.2.2 Governmental Organizations

3.2.2.1 In vivo Toxicity of Fullerenes

Title: Acute and subacute toxicity study of water-soluble polyalkylsulfonated C60 in rats.

Authors: Chen HH, Yu C, Ueng TH, Chen S, Chen BJ, Huang KJ, Chiang LY

Address: Dr. H. H. Chen

National Laboratory Animal Breeding and Research Center

National Science Council

Nankang, Taiwan

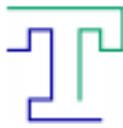
Date: January 1998

Source: Toxicol Pathol.; 26(1): pp143-151

Summary:

Many promising medical applications of fullerenes lead early on to studies investigating the toxicity of these special nanostructures. An example of such a animal toxicity study is listed here. These studies with rats treated with a polyalkylsulfonated fullerene (FC4S) revealed:

- FC4S was considered to be nontoxic if administered orally.
- Intraperitoneal injection showed toxicity in rats (LD50 ca. 600 mg/kg body weight).
- Intraperitoneally or intravenously injection eliminated the compound through the kidney. The compound induced kidney damage (lysosome-overload nephrosis, phagolysosomal nephropathy)
- The observed changes may serve as a biological marker in toxicity tests for this class of nanoparticles.



3.2.2.2 Relevance of Research on Ultrafine Particles for the Potential Toxicity of Engineered Nanoparticles

Because of occupational exposure to particles derived from industrial activities such as mining (e.g. coal) or more recently, due to increasing particulate urban air pollution, e.g. ultrafine particles (generally defined as particles in the size range < 100 nm) in exhaust of Diesel combustion engines, there is a large body of literature describing research on the association of airborne particles and adverse health effects. The question arises as to what extent the information gained from research on these ultrafine particles can be applied to the emerging class of new synthetic or engineered nanoparticles.

Title: Pulmonary effects of inhaled ultrafine particles.

Authors: Dr. Günther Oberdörster

Address: Department of Environmental Medicine
University of Rochester Medical Center
575 Elmwood Avenue
Rochester, NY 14642, USA

Tel: 001 716 275 3804

Fax: 001 716 256 2631

Email: gunter_oberdorster@urmc.rochester.edu

Date: November 2000

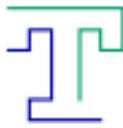
Source: Int Arch Occup Environ Health. 74(1): pp 1-8

Summary:

This review summarizes studies which led to the hypothesis that ultrafine particles (< 100 nanometer diameter) are causally involved in adverse responses seen in sensitive humans. Studies on rodents demonstrate that ultrafine particles administered to the lung cause a greater inflammatory response than do larger particles, per given mass. Surface properties (surface chemistry) appear to play an important role in ultrafine particle toxicity.

Note that Dr. Oberdörster is a renowned expert on inhalation toxicology who has been investigating effects and toxicokinetics of occupational and environmental particles for more than 25 years. More recently, his research has been focusing on ultrafine particles. As early as in 1985 he has published on the biological impacts of titanium dioxide particles on rats (Ferin and Oberdorster, 1985, Biological effects and toxicity assessment of titanium dioxides: anatase and rutile, Am. Ind. Hyg. Assoc. J., 46: pp 69-72). In addition, together with Dr. Mark Utell (University of Rochester School of Medicine, Rochester, New York) they formulated in 1994 the "ultrafine particle hypothesis" stating that airborne ultrafine particles may cause adverse health effects.

A more recent Editorial by Oberdörster and Utell in the Journal Environmental Health Perspectives (2002 Aug.; vol.110(8), A440-441) also addresses the intriguing questions of transport processes of ultrafine particles:



- across the blood-brain barrier (Kreuter J. 2001. Nanoparticulate systems for brain delivery of drugs. *Adv Drug Delivery Rev* 47, pp 65-81; see also chapter 3.2.2.6 herein)
- from lung tissue to the blood stream (Gumbelton M. 2001. Caveolae as potential macromolecule trafficking compartments within alveolar epithelium. *Adv Drug Delivery Rev* 49, pp 281-300)
- from the respiratory tract to the central nervous system (CNS): In 1940, Howe and Bodian described for the first time such a transport processes for the poliomyelitis virus (30 nm) in monkeys (Howe HA and Bodian D. 1940. Portals of entry of poliomyelitis virus in the chimpanzee. *Proc Soc Exp Biol Med* 43, pp718-721). Later on, similar findings were reported for colloidal gold particles (50 nm) moving from the nose to neuronal tissue (olfactory bulb) of monkeys (De Lorenzo A., Darin J. 1970. The olfactory neuron and the blood-brain barrier. In: *Taste and Smell in Vertebrates* (Wolstenholme GEW, Knight J. eds.) London:Churchill, pp151-176).

Title: Particle Toxicology: from coal mining to nanotechnology.

Authors: Prof. Dr. Paul J. A. Borm

Address: Center of Expertise in Life Sciences (CEL)

Hogeschool Zuyd

PO Box 550

6400 AN HEERLEN, The Netherlands

Tel: 0031 45 400 6436

Mobile: 0031 64 172 5351

Email: p.borm@hszuyd.nl

Web: www.hszuyd.nl

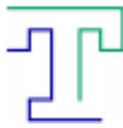
Date: March 2002

Source: *Inhal. Toxicol.*;14(3): pp 311-324

Summary:

This article reviews particle research with a historical perspective of industrial activities and materials (coal, asbestos, man-made mineral fibers, ambient particulate matter). More specifically, the major differences between historical and current research in particle toxicology are summarized:

- the exposure concentrations (from 2-5 mg/m³ to 20-50 mg/m³)
- particle size (from 1-2 µm to 20-100 nm)
- target populations
- endpoints
- length of exposure



- effects of inhaled particles due to their suggested translocation to the blood
- use of certain nanoparticles as carriers in medical applications
- organizations sponsoring particle toxicology research in Europe

The author encourages a link between toxicology and technology development to learn more about potential risks and about the role of surface and size in particle toxicity.

Title: ETH Conferences on Combustion Generated Particles

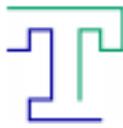
Authors: several, see Appendix

Date: August 2003

Source: http://www.nanoparticles.ethz.ch/haupt/link.dir/frame_nano.htm

Summary:

To illustrate the importance of research on combustion generated particles, the ETH in Zürich has been organizing an ongoing series of conferences on this topic. The content section of the Book of Abstracts prepared for the 7th ETH Conference on Combustion Generated Particles is reproduced in the Appendix section of this report (chapter 7.2). Note that these conferences were formerly known as "ETH Conference on Nanoparticle-Measurement".



3.2.2.3 First U.S. Report on Societal Implications of Nanotechnology

Title: Societal Implications of Nanoscience and Nanotechnology

Editors: Mihail C. Roco and William Sims Bainbridge

Address: Dr. Mihail C. Roco

Senior Advisor, National Science Foundation

4201 Wilson Blvd

Arlington, VA 22230, USA

Tel: 001 703 292 8301

Fax: 001 703 292 9013

Email: mroco@nsf.gov

Web: www.nsf.gov/nano

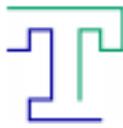
Date: March 2001

Source: <http://www.nsf.gov/home/crssprgm/nano/nsfnireports.htm>

Summary:

This first U.S. report on societal implications of nanotechnology integrates the views and opinions of leading experts from academia, private sector and government. The report was published as a result of the workshop "Societal Implications of Nanoscience and Nanotechnology" held on Sept 28-29 2000 at the National Science Foundation. This workshop was sponsored by the Subcommittee on Nanoscale Science, Engineering, and Technology (NSET) of the U.S. National Science and Technology Council (NSTC), the principal means for the U.S. President to coordinate science, space and technology policies across the Federal Government. The following recommendations were proposed by the workshop participants and other leading experts:

- Support social and economic research studies on nanotechnology with high priority.
- The National Nanotechnology Coordination Office (NNCO) should promote the information, education and the involvement of the public regarding the potential impacts of nanotechnology.
- Creation of the knowledge base and the institutional infrastructure to evaluate the scientific, technological and societal impacts with short term (3 to 5 year), medium-term (5 to 20 year) and long-term (over 20 year) perspectives.
- Education and training of a new generation of scientists and workers skilled in nanoscience and nanotechnology.
- To encourage professional societies to set up forums and continuing education programs to inform and educate nanoscience and nanotechnology professionals.



3.2.2.4 In vitro Cytotoxicity of Nanoparticles

Title: Photo-induced cytotoxicity of malonic acid [C(60)]fullerene derivatives and its mechanism.

Authors: Yang XL, Fan CH, Zhu HS

Address: Dr. X. L. Yang
Research Center of Materials Science
Beijing Institute of Technology
P.O. Box 327
Beijing 100081, PR China.

Email: xlyang@bit.edu.cn

Date: February 2002

Source: Toxicol In Vitro; 16(1): pp 41-46

Summary:

As a consequence of their promising medical applications, based on their unique free-radical chemistry, the biological activities of water-soluble fullerenes have attracted extensive attention in recent years. The aim of this paper is to study the relation of the photo-induced cytotoxicity of fullerene derivatives to their chemical structures as well as the possible cellular mechanism involved in the photocytotoxicity.

Title: Effects of hydroxyapatite nanoparticles on proliferation and apoptosis of human hepatoma BEL-7402 cells

Authors: Zhi-Su Liu, Sheng-Li Tang, Zhong-Li Ai

Address: Dr. Zhi-Su Liu
Department of General Surgery
Zhongnan Hospital of Wuhan University
Wuhan 430071, Hubei Province, China

Tel: + 86 27 87331752

Fax: + 86 27 87330795

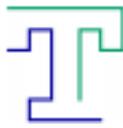
Email: hyfr@mail.wh.cei.gov.cn

Date: September 2003

Source: World J Gastroenterol, 2003; 9(9):pp1968-1971

Summary:

In vitro cytotoxicity of hydroxyapatite (HAP) nanoparticles (with 50 nm diameter) on a human hepatoma (liver cancer) cell line was investigated. Treatment of these human liver cells lead to dose-dependent growth inhibition (IC₅₀= 29 µg/ml) and induction of apoptosis (= programmed cell death).



Title: Surface-engineered nanoparticles for multiple ligand coupling

Authors: Gref R, Couvreur P, Barratt G, Mysiakine E

Address: Dr. R. Gref

School of Pharmacy

UMR CNRS

University of Paris Sud

5, Rue J.B. Clement

Chatenay Malabry 8612, France

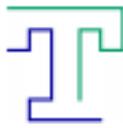
Email: ruxandra.gref@cep.u-psud.fr

Date: November 2003

Source: Biomaterials. 2003 Nov; 24(24):pp 4529-4537

Summary:

In the course of studies aiming at engineering the surface of biodegradable nanoparticles for drug targeting applications, the cytotoxicity of such 100 nm nanoparticles was investigated. In vitro experiments with Caco-2 cells indicated that the cytotoxicity of these poly(ethylene glycol)-poly(epsilon-caprolactone) co-polymer nanoparticles was negligible (> 80% cell survival for nanoparticle concentrations up to ca 1000 µg/ml).



3.2.2.5 Toxicology Aspects of Nanoparticles in Sunscreens

Title: Distribution of sunscreens on skin.

Authors: Schulz J, Hohenberg H, Pflucker F, Gartner E, Will T, Pfeiffer S, Wepf R, Wendel V, Gers-Barlag H, Wittern KP.

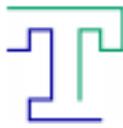
Address: Dr. Jens Schulz
R&D Cosmed
Beiersdorf AG, Function 4243
Unnastrasse 48
D-20245, Hamburg, Germany
Tel: 0049 (40) 4909 0
Fax: 0049 (40) 4909 3434
Email: jens.schulz@beiersdorf.com
Web: www.beiersdorf.com

Date: November 2002

Source: Adv Drug Deliv Rev.; 54(1): pp 157-163

Summary:

Absorption of micronised pigments, such as titanium dioxide or zinc oxide nanoparticles, has been investigated. This publication demonstrates that neither surface characteristics, particle size nor shape of the micronised pigments result in any dermal absorption of these particles. Micronised titanium dioxide is solely deposited on the outermost surface of the stratum corneum and cannot be detected in deeper stratum corneum layers, the human epidermis and dermis.



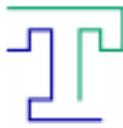
3.2.2.6 Toxicology Aspects of Nanoparticles in Drug Delivery

- Title:** Direct evidence that polysorbate-80-coated poly(butylcyanoacrylate) nanoparticles deliver drugs to the CNS via specific mechanisms requiring prior binding of drug to the nanoparticles.
- Authors:** Kreuter J, Ramge P, Petrov V, Hamm S, Gelperina SE, Engelhardt B, Alyautdin R, von Briesen H, Begley DJ.
- Address:** Prof. Dr. Jörg Kreuter
Institut für Pharmazeutische Technologie
Biozentrum
J.W. Goethe-Universität
Frankfurt, Germany
Tel: 0049(69)798-29682
Fax: 0049(69)798-29694
Email: Kreuter@em.uni-frankfurt.de
- Date:** March 2003
- Source:** Pharm Res.; 20(3): pp 409-416

Summary:

This study addresses the question of whether the poly(butylcyanoacrylate) (PBCA) nanoparticle drug delivery system has a generalized toxic effect on the blood-brain barrier (BBB), as has been suggested recently. The results of in vitro and animal experiments suggest that these nanoparticles do not simply disrupt the BBB and thereby promote uptake of the nanoparticles into the brain.

Note that similar PBCA nanoparticles are currently being investigated pre-clinically as a novel drug delivery system for brain cancer (www.advectuslifesciences.com).



3.2.2.7 Report for the Swiss "Zentrum für Technologiefolgen-Abschätzung"

Title: Technologiefolgen-Abschätzung zur Nanotechnologie in der Medizin.
Überarbeiteter Entwurf des Schlussberichtes.

Author: Dr. Walter Baumgartner

Address: Basics AG; Entscheidungsgrundlagen für Politik und Wirtschaft
Beckenhofstrasse 16
Postfach 176
8035 Zürich, Switzerland
Tel: 01 362 99 00
Web: www.basics.ch

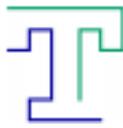
Date: June 2003

Source: This study was carried out on behalf of the Swiss "Zentrum für Technologiefolgen-Abschätzung beim schweizerischen Wissenschaftsrat".

Summary:

The goal of this study is to anticipate possible impacts of nanotechnology on medical practice within the next twenty years. To this end, a "Delphi" approach was chosen and more than 70 experts in the field of nanotechnology were interviewed. The following sections of the final report are relevant within the scope of this survey.

- **"Risiken"** (pp 43-46): Toxicological risks of medical applications of nanotechnology was estimated to be "considerable" by the expert team (on a six-step scale, ranging from "negligible" to "very high").
- **"Ethische Überlegungen"** (pp 44-66): Two viewpoints; for one group of experts there are principally no ethically motivated restrictions of nanotechnology in medicine, except sensitive issues concerning .g. brain physiological ("neuro-chips") and eugenics-type of applications. The second group puts forward more fundamental ethical and moral concerns regarding nanotechnology application in medicine with a reasoning similar to the actual debates relating to cloning, stem cell and gene therapy applications in humans.
- **"Missbrauchsrisiken"** (pp 71-72): Enhancement of ongoing discussions regarding genetic analysis and manipulation of individuals propelled through more efficient and less costly nano-biotechnological methods (key word: "massively parallel genomics").
- **"Empfehlungen"** (pp 84-85): The findings gained from this study are condensed in seven "thesis", from which #3 to #7 deal with potential risks of the application of nanotechnology in medicine.



3.2.2.8 Review on Technical Aspects of Nano-Toxicology

Title: The potential environmental impact of engineered nanomaterials.

Author: Dr. Vicki Colvin

Address: Department of Chemistry and Chemical Engineering
Center for Biological and Environmental Nanotechnology (CBEN)
MS-60 Main Street
Rice University
Houston, Texas 77005, USA
Tel: 001 713-348 5741
Email: colvin@ruf.rice.edu

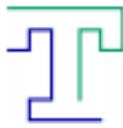
Date: October 2003

Source: Nature Biotechnology, Volume 21, Number 10, pp1166-1170

Summary:

This recent publication represents the viewpoint of the nano-scientist in charge of establishing a framework for an assessment methodology for engineered nanomaterials. Clearly, there is a relative lack of data on the biological effects of engineered nanomaterials. However, publications are emerging that address the toxicology of carbon nanostructures (fullerenes and carbon nanotubes) due to the promising medical applications of fullerenes, several in vitro and animal toxicology studies have been performed so far.

Importantly, this article contains a very useful reference index of publications investigating the toxicity of nanoparticles, including references on Ultra Fine Particles (UFPs) whose toxicological characteristics have been studied for much longer.



3.2.2.9 Emerging Toxicity Data on Carbon Nanotubes

Title: Comparative Pulmonary Toxicity Assessment of Single Wall Carbon Nanotubes in Rats.

Authors: Warheit DB, Laurence BR, Reed KL, Roach DH, Reynolds GA, Webb TR.

Address: Dr. David B. Warheit
DuPont Haskell Laboratory
P.O. Box 50
Elkton Road
Newark, Delaware, USA
Email: david.b.warheit@usa.dupont.com

Date: Sept 26, 2003 (Epub ahead of print), in the press

Source: Toxicol. Sci. (www.toxsci.oupjournals.org)

Summary:

This study, one of the first peer-reviewed toxicological studies of single-walled carbon nanotubes (SWCNT), investigated the acute lung toxicity of SWCNT in rats. The lungs of rats were instilled either with the following control or particle-types:

- 1) SWCNT
- 2) Quartz particles (positive control)
- 3) Carbonyl iron particles (negative control)
- 4) Phosphate-buffered saline + 1% Tween 80 (vehicle control)
- 5) Graphite particles

The lungs of treated rats were assessed using biomarkers, cell proliferation methods, and by histopathological evaluation of lung tissue at 24 hrs, 1 week, 1 month and 3 months post-instillation exposure.

At high exposure doses, SWCNT produced mortality in approximately 15% of the treated rats (within 24 h). Interestingly, the mortality resulted from mechanical blockage of the upper airways by the instilled nanotubes, and was not due to pulmonary toxicity of the SWCNT.

However several inconsistencies of the toxicity data were observed. "In addition, the results of two recent exposure assessment studies indicate very low aerosol SWCNT exposures at the workplace. Thus, the physiological relevance of these findings should ultimately be determined by conducting an inhalation toxicity study."



Title: Pulmonary Toxicity of Single-Wall Carbon Nanotubes in Mice 7 and 90 Days after Intratracheal Instillation.

Authors: Lam CW, James JT, McCluskey R, Hunter RL.

Address: Dr. Chiu-Wing Lam

Wyle Laboratories
NASA Johnson Space Center
1290 Hercules Dr., Suite 120
Houston, Texas 77058, USA

Tel: 001 281 212 1200

Fax: 001 281 212 1210

Email: Chiu-wing.Lam@jsc.nasa.gov

Dr. Robert L. Hunter, Jr.

Department of Pathology
University of Texas-Houston
Medical School

6431 Fannin

Houston, TX 77030, USA

Tel: 001 713 500 5301

Fax: 001 713 500 0732

Email: Robert.L.Hunter@uth.tmc.edu

Date: Sept 26 2003 (Epub ahead of print), in the press

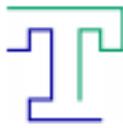
Source: Toxicol. Sci. (www.toxsci.oupjournals.org)

Summary:

Since unprocessed nanotubes are very light, they could become airborne and potentially reach the lungs. This is one of the first peer-reviewed toxicological studies of well characterized single-walled carbon nanotubes. Three different types of single-wall carbon nanotubes containing different amounts of residual catalytic metals were studied. Mice were intratracheally instilled with nanotubes, a carbon black negative control, or a quartz positive control, and their lungs were histopathologically analyzed 7 d or 90 d after the treatment. All nanotubes induced dose-dependent epithelioid granulomas, a combination of dead and live tissue surrounding the nanotubes, in lungs of exposed mice and in some cases interstitial inflammation. The lungs of mice treated with carbon black were normal, whereas those treated with high-dose quartz revealed mild to moderate inflammation.

"These results show that, for the test conditions described here and on an equal-weight basis, if carbon nanotubes reach the lungs, they are much more toxic than carbon black and can be more toxic than quartz, which is considered a serious occupational health hazard in chronic inhalation exposures."

However, critics of this study point out that it is unclear at the moment whether this response was caused by the nanotubes or by the metal catalyst particles present in the sample.



3.2.2.10 Additional Medical Issues

Further information on additional topics will be added, as soon as publications relevant to nanoparticles as defined in Chapter 1.1 are available. Preliminary literature searches revealed mainly studies investigating the impact of Ultrafine Particles relevant to the following topics:

- macrophage overload
- free radicals
- enzyme - nanoparticle interactions (modulation of enzyme activity by nanoparticles)

However, a prominent example of enzyme inhibition by nanoparticles is exemplified by fullerenes which are known to inhibit the reverse transcriptase and protease enzymes of Human Immunodeficiency Virus (HIV), as described for example in the following study.

Title: Pharmacokinetics of a Water-Soluble Fullerene in Rats

Authors: Rajagopalan P, Wudl F, Schinazi RF, Boudinot FD

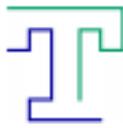
Address: Dr. F. Douglas Boudinot
Department of Pharmaceutics
University of Georgia
Athens, Georgia 30602-2353, USA
Tel: 001 706 542 5335
Fax: 001 706 542 5346
Email: boudinot@rx.uga.edu

Date: Oct. 1996

Source: Antimicrobial Agents and Chemotherapy, Vol 40, No 10, pp2262-2265

Summary:

One of the first pharmacokinetic studies of a fullerene derivative with anti-HIV activity in rats. The therapeutic window of this compound seems to be quite narrow, since this fulleren was well tolerated at 15 mg/kg, whereas at 25 mg/ml, the animals died within 5 min. after intravenous administration of the compound.



3.3 Selected Newspaper Articles on Risks of Nanotechnology

3.3.1 Swiss Press

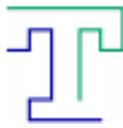
3.3.1.1 Recent Articles by the Swiss Science Journalist Barbara Vonarburg

Title: Schrecklich schöne neue Welt
Author: Barbara Vonarburg
Address: Redaktion Tages-Anzeiger
Werdstrasse 21
8004 Zürich
Tel: 01 248 44 11
Fax: 01 248 44 71
Email: barbara.vonarburg@tages-anzeiger.ch
Date: June 24, 2003
Source: Tagesanzeiger, p 68

Summary:

This article discusses the following issues:

- Self-replicating nanorobots (i.e. "grey goo" by Michael Crichton).
- Nanoparticles in sunscreen lotions and their unknown health risk.
- Are nanotubes as toxic as asbestos? (ref. NewScientist, No 2388, p14)
- Reference to ETC reports and proposed moratorium for nanotechnology.
- Reference to EMPA meeting in Dübendorf (June 18, 2003) "Nano zwischen Zweifel und Zuversicht".
- Mrs Vonarburg pleads in an accompanying commentary for more funding of risk assessment studies (quote: "64 mio CHF funding for four years of the Center of Competence for Nanoscience in Basel versus 80'000 CHF for a study on impacts of nanotechnology in medicine", see 3.2.2.5 of this report).

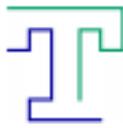


Title: Ein Jahrmarkt der Nanotechnologie
Author: Barbara Vonarburg
Address: Redaktion Tages-Anzeiger
Werdstrasse 21
8004 Zürich
Tel: 01 248 44 11
Fax: 01 248 44 71
Email: barbara.vonarburg@tages-anzeiger.ch
Date: September 9, 2003
Source: Tagesanzeiger, p 42

Summary:

This article is primarily about the Nanofair and Nano-Conference which took place in September 2003 in St. Gallen. However, one section is about the potential risks of nanotechnology with two quotes of Nobel laureate Heinrich Rohrer:

- "Welchen Einfluss haben Nanomaterialien auf unsere Gesundheit? Das wird eine der zentralen Fragen sein."
- "Es wird eine der grössten Herausforderungen sein, herauszufinden, was die Nanopartikel in biologischen Systemen Nützliches und Schädliches bewirken."



3.3.1.2 Viewpoint of an Insurance Company

Title: Kleine Dinge - grosse Wirkung? Die Nanotechnologie aus der Sicht der Versicherung

Authors: Annabelle Hett and Rolf Tanner

Address: Dr. Annabelle Hett

Risk Specialist

Swiss Re

Mythenquai 50/60

P.O. Box

8022 Zurich, Switzerland

Tel: 043 285 2121

Fax: 043 285 2999

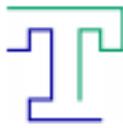
Web: www.swissre.com

Date: September 30, 2003

Source: Neue Zürcher Zeitung, Nr. 226, p 15

Summary:

For insurance companies it is important to get benchmark figures for what kind of damage a new technology can cause, respectively what the extend and incidence of such damage will be. Since engineered nanomaterials are already used in industry and for consumer products, insurance companies need to assess the overall risks of nanotechnology.



3.3.2 International Press

3.3.2.1 NewScientist Article

Title: How safe is nanotech?
Authors: Kurt Kleiner and Jenny Hogan
Address: NewScientist
Web: www.newscientist.com
Date: March 29, 2003
Source: New Scientist, vol 177, issue 2388, pp 14-16

Summary:

The information on health risks of nanotubes is mainly based on data presented at a meeting of the American Chemical Society held in New Orleans, March 23-27 2003. Two studies were presented, which examined the effect of nanotubes on lung tissue of rats and mice:

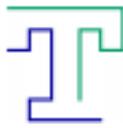
- Chiu-Wing Lam (Wyle Laboratories of NASA's Johnson Space Center, Houston, Texas) and Robert Hunter (University of Texas, Houston Health Science Center) placed a few drops of a suspension of nanotubes, directly into the lungs of mice. These nanotubes clumped together into bundles, and the bundles were invariably surrounded by immune cells (macrophages). This so-called "foreign body response" left scar tissue, damaging the original lung tissue.

Dr. Hunter was cited in this NewScientist article: "People should really take precautions. Nanotubes can be highly toxic. There's variability between different nanotubes and very little is known about it." Part of this quote made it even into Barbara Vonarburg's Tages-Anzeiger article "Schrecklich schöne neue Welt".

Note that the data presented at this meeting in March 2003 is now accepted for publication in a peer-reviewed toxicology journal (see 3.2.2.9).

- Results of a similar toxicology study investigating the effects of single wall carbon nanotubes on lung tissue of rats were presented by David Warheit (DuPont's Haskell Laboratory in Newark, Delaware, USA) at the American Chemical Society meeting in New Orleans. Similarly, these authors also found immune cells accumulated around clumps of nanotubes in lungs of treated rats. In addition, at the highest dose, several rats died most probably because the nanotubes had clumped together in their lungs such that these animals suffocated.

Note that the data presented at this meeting in March 2003 is now accepted for publication in a peer-reviewed toxicology journal (see 3.2.2.9).



3.4 International Research Projects on Risk Assessment of Nanotechnology

3.4.1 U.S. Projects

3.4.1.1 National Nanotechnology Initiative (NNI)

Title: Broader societal issues of nanotechnology
Contact: Dr. Mihail C. Roco
Address: National Science Foundation
National Science and Technology Council's Subcommittee on Nanoscale Science
4201 Wilson Blvd.
Arlington, VA 22230, USA
Tel: 001 703 292 8301
Fax: 001 703 292 9013
Email: mroco@nsf.gov
Web: www.nsf.gov/nano
Date: March 2003
Source: Journal of Nanoparticle Research, vol. 5; pp 181-189

Summary:

This publication gives a valuable outline of the US National Nanotechnology Initiative (NNI) annual investment in research with educational, societal, environmental and health implications. The total annual NNI research funding aiming at supporting investigations on societal implications of nanotechnology is estimated at about \$30 million. Of this financial support, about \$23 million are awarded through the US National Science Foundation (NSF). In addition, nanoscale research with relevance to environmental and health issues is supported with about \$50 million annual funding. In this area, the NSF awards about \$30 million and the U.S. Environmental Protection Agency (EPA) about \$6 million.

To illustrate the type of research projects and research centers which are supported by NNI, Table 3 of Dr. Roco's publication is shown below (with kind permission of the author).



Table 3. Examples of NSF awards for nanoscale processes in the environment: Understanding the implications

Topic	University (lead investigator)	Interval
Nanoparticles in the environment, agriculture and technology	UC Davis (A. Novrotski), IGERT	1999–2004
Nanoparticle formation in air pollution	WPI (B.E. Wyslouzil)	2000–2005
Nanoparticle science and engineering	U. of Minnesota (U. Kortshagen), IGERT	2001–2006
Nano-colloids (metals, actinides) in aquatic systems	TAMU (P. Santschi), NIRT; and U. Notre Dame (J.B. Fein, Environmental Molecular Science Institute)	2001–2005
Surface reactivity of nanostructures in environment	UCB (J.F. Banfield), U. Vanderbilt (P.T. Cummins), TX Tech University (M.K. Ridley), NIRT	2001–2005
Application of quantum dots to environment and cell biology	Lehigh U. (A.K. Sengupta)	2001–2004
Molecular minerals–microbial interactions in the environment	U. Oklahoma (M. Nanny), (NIRT); U. Virginia (M.F. Hochella)	2001–2005
Biological and environmental nanotechnology	Rice U. (V. Colvin), NSEC	2001–2006

3.4.1.2 U.S. Environmental Protection Agency (EPA)

Title: **Impacts of Manufactured Nanomaterials on Human Health and the Environment**

Contact: **Dr. Barbara Karn**
(in charge of directing nanotechnology research at EPA)

Address: U.S. Environmental Protection Agency (EPA)
Office of Research and Development
National Center for Environmental Research
Washington, DC 20460, USA

Tel: 001 202 564 6824

Email: karn.barbara@epa.gov

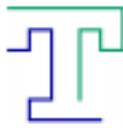
Web: <http://es.epa.gov>

Date: July 2003 (Opening date for research proposals)

Source: U.S. Environmental Protection Agency (EPA)

Summary:

The research program of the U.S. Environmental Protection Agency (EPA) invites for research proposals that focus on potential toxicity of and exposure to manufactured nanomaterials (nanoparticles, nanotubes, nanowires, and others). An estimated number of 12 awards is expected with a total anticipated funding amount of approximately \$4.0 million.



The published due date for the research proposals is December 11, 2003. Therefore, the research projects will not commence before mid 2004.

Research topics to be addressed in this program include:

1. Toxicology of manufactured nanomaterials:

What is the toxicity or potential toxicity of manufactured nanomaterials?

Can similar nanomaterials be grouped with respect to their bioactivity?

What are the dose-response characteristics of nanomaterials?

What are appropriate testing procedures to evaluate the potential toxicological effects of nanomaterials?

What extrapolation models are needed to evaluate or predict toxicity?

What is the mode of action and mechanism of toxicity?

What effects may occur in exposed human populations?

Are some subpopulations more sensitive to nanomaterials?

2. Environmental and biological fate, transport, and transformation of manufactured nanomaterials:

By what means do (can) manufactured nanomaterials enter the environment?

What are the modes of dispersion for nanomaterials in the environment?

Do manufactured nanoparticles undergo transformation in the environment?

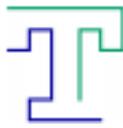
3. Exposure and bioavailability of manufactured nanomaterials:

How and to what degree are humans exposed to nanomaterials in the environment?

What effects may occur in exposed human populations?

Are some subpopulations more vulnerable to nanomaterial exposure?

What are the exposure pathways for humans?



3.4.2 European Projects

3.4.2.1 NANO-PATHOLOGY Project

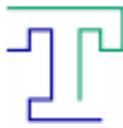
- Title:** The role of nano-particles in material-induced pathologies
- Contact:** Manuela Arata ("Prime Contractor")
- Address:** Italian Institute for the Physics of Matter
Laboratorio dei Biomateriali
Università di Modena e Reggio Emilia, Modena, Italia
Via del Pozzo 71
41100 Modena, Italy
Tel: 0039 1 0659 8740
Fax: 0039 1 0650 6302
Email: arata@infm.it
Web: www.infm.it
- Date:** December 2001 (Start date)
- Source:** The NANO-PATHOLOGY project is part of the 5th Fifth Framework Programme of the European Commission (Program Acronym: LIFE QUALITY).

Summary:

The goals of the NANO-PATHOLOGY project are the following:

- to develop diagnostic methods and tools for the detection of micro- and nanoparticles relevant for pathological processes of unknown etiology
- to investigate patho-mechanisms of possible particle-induced disease by using suitable animal experimentation and in vitro models
- to determine the pathological significance of nanoparticles

The NANO-PATHOLOGY project involves 5 research partners including 3 academic institutions and two industry organizations. The project started December 1 2001 with a duration of 3 years and has received EU funding of ca. Euro 1 million.



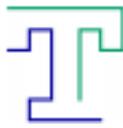
3.4.2.2 NANODERM Project

Title: Quality of skin as a barrier to ultra-fine particles
Contact: Peter Gutjahr-Löser ("Prime Contractor")
Address: Faculty of Physics and Geosciences
Universität Leipzig
Linnestrasse 5
P.O. Box 100 920
04103 Leipzig, Germany
Tel: 0049 341 97-30100
Fax: 0049 341 97-30109
E-Mail: kanzler@uni-leipzig.de
Web: www.uni-leipzig.de
Date: January 2003 (Start date)
Source: The NANODERM project is part of the 5th Fifth Framework Programme of the European Commission (Program Acronym: LIFE QUALITY).

Summary:

This study investigates the fate of nanoparticles currently used for body care and household products. The major question to be answered by this study is how deep these ultrafine particles (e.g. < 20 nm TiO_2) penetrate the horny layer of the skin and possibly underlying dermal layers. To this end, ultra-sensitive microscopy methods will be employed in conjunction with radio-labeled Ti particles. In addition, pathways of percutaneous uptake and clearance, particle-tissue as well as particle-cell interactions will be investigated.

The NANODERM project involves 7 research partners including 4 academic institutions and 3 research organizations. The project started January 1 2003, with a duration of 3 years and has received EU funding of Euro 1.1 million.



3.4.2.3 NANOSAFE Project

Title: Risk Assessment in Production and Use of Nanoparticles with Development of Preventive Measures and Practice Codes

Contact: Dr. Rüdiger Nass ("Prime Contractor")

Address: NANOGATE Technologies GmbH
Gewerbepark Eschberger Weg
66121 Saarbrücken, Germany

Tel: 0049-681 9805211

Fax: 0049-681 9805252

Email: ruediger.nass@nanogate.com

Web: www.nanogate.de

Date: April 2003 (Start date)

Source: The NANOSAFE project is part of the 5th Fifth Framework Programme of the European Commission (Program Acronym: GROWTH).

Summary:

The NANOSAFE project deals with the assessment of risks involved in production, handling and use of nanoparticles in industrial processes and products, as well as in consumer products.

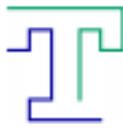
The NANOSAFE project involves 9 research partners including:

- laboratories developing nanoparticles or materials
- companies presently making or using nano materials
- medical research laboratories in pneumology and epidemiology
- a large national industry professional association.

The project started April 1 2003 with a duration of 15 months and has received EU funding of ca. Euro 300,000. At the conclusion of the project a Conference will be held for presentation of the results and recommendations, including proposed regulations, preventive measures and codes of good practice.

3.4.2.4 Further EU Projects

Further calls for research proposals within the Sixth Framework Programme of the European Union, aiming at understanding the "impact of nanoparticles on human health and the environment" are scheduled for November 30, 2003.



3.5 Voices from the European Community

3.5.1 European Parliament: First Seminar on Societal Impacts of Nanotechnology

Title: Nanotechnology: opportunity or threat?
Address: CORDIS Community Research & Development Information Service
Web: <http://www.cordis.lu/en/home.html>
Date: June 11, 2003
Source: http://dbs.cordis.lu/fep-cgi/srchidadb?ACTION=D&SESSION=297952003-10-22&DOC=1&TBL=EN_NEWS&RCN=EN_RCN_ID:20401&CALLER=EN_NEWS

Original Text:

Innovation is running ahead of regulation, claimed UK MEP Caroline Lucas at the first ever international seminar on the societal impacts of nanotechnology, held at the European Parliament on 11 June.

Nanotechnology is a new manufacturing technology able to make products smaller and stronger. The particles used in nanotechnology research or manufacturing are invisible to the human eye, one nanometer being one billionth of a meter. A human hair is 80,000 nanometers wide.

While participants recognized the benefits that the nanotechnology revolution could bring, most had concerns. This apprehension was not restricted to one field, but covered human health, environmental impacts, effects on international trade and developing countries, and the possible proliferation in armaments. The main concern expressed by those present however, was that we just do not know what the impacts of nanotechnology will be. It is this lack of knowledge that led some participants to call for a moratorium on certain aspects of nanotechnology use and research.

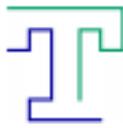
'I am not against new technologies, but want to be sure of their impact,' said Dr Lucas, who claimed that 'the minimum that we need now is a moratorium on products applied to the skin,' a proposal supported by several other speakers.

Although most people do not realize it, we are already surrounded by products developed using nanotechnology. Face creams and sun tan lotions are two examples, and according to Dr Lucas, there is evidence that such creams, which are able to pass through the skin, are potentially mutagenic and cancerous.

These health concerns were echoed by Vyvyan Howard, a toxicologist from the University of Liverpool in the UK. Nanoparticles can pass into the body by three means, he explained: through inhalation and ingestion, and transdermally.

'Breathing in very small particles has toxic effects, and it doesn't seem to matter what they're made of,' said Dr Howard. The important thing is size, he said, pointing to concerns about particles between 65 and 200 nanometers in size - the toxicity increases as the size of the particle decreases.

'Another worry is where the particles get to within the body,' said Dr Howard. We know from pharmaceutical companies that putting a drug on the back of a nanoparticle can increase the delivery of the drug to the brain. 'If it [the nanoparticle] can get to the brain,



I see no reason why it wouldn't get to the foetus,' said Dr Howard. He called for more research on such implications and called on scientists to work together: 'Groups of scientists are working independently. They don't seem to be talking, and I think they must.'

One way of increasing such collaboration is through the European Commission's Sixth Framework Programme, where nanotechnology features as one of the thematic priorities and has accordingly been allocated a budget of 1,300 million euro for the years 2003 to 2006. Head of Unit for nanotechnology within the Commission, Renzo Tomellini explained that the Commission's aim in funding such research is to create new economic opportunities and improve living conditions for Europe's citizens.

Mr Tomellini recognized concerns about the implications of nanotechnology, and stressed that if a danger is perceived, it needs to be investigated.

Jürgen Altmann, from the University of Dortmund, drew attention to the possible impact that nanotechnology could have on military operations. Research is already being conducted by the military, and has been since as early as the 1980s. There has been a recent increase in such activity, particularly in the US, said Dr Altmann.

Researchers in the US are currently working on a battle suit that would protect soldiers from radiation and also act as a compress when a soldier is injured, said Dr Altmann. Other innovations could include the facilitation of surveillance, bombs the size of a pen that could flatten a whole city and, most worryingly for Dr Altmann, the manipulation of the human body to make soldiers more stress-tolerant, to repair injuries more effectively and to speed up reactions. Dr Altmann is also concerned that once such technology has been used by the military, the transfer to civilian life will be a natural step. He called for a moratorium on non medically-driven implants.

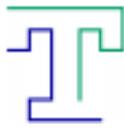
Dr Altmann also called for a slowing down by the US, which is at the forefront of such research, saying: 'The US is way ahead and so won't lose anything with a slow deceleration and it could buy time for an international agreement on limits [to such technology].'

The need for deceleration and investigation was also highlighted by Pat Mooney, Executive Director of the action group on erosion, technology and concentration (etc). 'Do policy makers know this technology is coming?' asked Mr Mooney. 'Most have no idea, and it's not only coming, it's here,' he said. He claimed that governments are currently running around five years behind time in terms of assessing the potential impacts.

'As much as health and environmental concerns must be a priority, there is a desperate need to look at the effects on and control of the economy,' said Mr Mooney, highlighting his main concern. Nanotechnology will mean that the raw materials that we currently consider to be essential will change, and that this will have a dramatic effect on developing countries, many of which rely on the export of raw materials.

The effect on developing countries was also highlighted by Vandana Shiva from the Indian Research Foundation on Science and Technology. She criticized the way in which some countries are being told that they must become nano-adapted, or remain underdeveloped. Dr Vandana also criticized the way in which nanotechnology is being used: 'The way in which nanotechnologies are being presented is a betrayal of the science on which they are based. At a time when science allows us to see the world in a deeper way, the quantum is brushed aside by the uses of the science,' she claimed.

Mr Mooney also expressed concerns about the impact on intellectual property, as it is conceivable that a single patent may have dominance over many industrial sectors as it could cover the fundamentals of all matters. 'This avoids most of the debates which have



taken place on patenting life because this goes below the level of life. This concerns the ownership of nature,' said Mr Mooney.

Mr Mooney also warned that 'the coalition between industry and government will get worse. It will protect the interests of what they say is society, but what they mean is industry.'

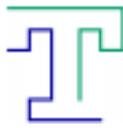
Mr Mooney also pointed to the different ways in which researchers are handling nanoparticles as justification for slowing down and taking stock of nanotechnology. While scientists in South Africa handle nanoparticles as if they were dealing with the AIDS virus, other researchers, including some in Europe, wear only a 'Japanese subway mask' as protection. 'This is like wearing a volleyball net to keep out mosquitoes,' said Mr Mooney.

Chief scientist with Greenpeace in the UK, Doug Parr drew comparisons between this new controversy and the recent debate on genetically modified organisms (GMOs). Policy makers' consideration of GMOs was originally very narrow, claimed Dr Parr. An overall policy lesson should be that policy must not be composed by small groups of experts and bureaucrats, he claimed. He called on the EU to act as a technology facilitator with a user or civil society forum.

The need for further research has already been recognized by the UK government, which requested a study on the potential benefits and problems on 11 June.

Although many possible dangers were highlighted at the Parliament conference, including the fear of autonomous self-replicating nanorobots, a number of possible benefits were also acknowledged. Products such as self-cleaning trousers and crack-resistant paint are already on the market, and future applications could allow the removal of the smallest contaminants, including greenhouse gases in the atmosphere.

Summing up the conference, Dr Lucas recommended that policy makers ensure they are asking the right questions, and stressed that the 'most immediate priority is to prevent those who have the most to gain - big business - from beating the regulation race.' She claimed that this is unlikely to happen in the EU without a huge amount of pressure, and called on the Commission to mainstream safety concerns.



3.5.2 European Commission: Interview with Dr. Renzo Tomellini

Title: Supporting responsible nanotechnology research will benefit Europe's citizens, says head of unit

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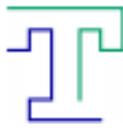
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Date: June 26, 2003

Source: http://dbs.cordis.lu/fep-cgi/srchidadb?ACTION=D&SESSION=269672003-10-22&DOC=1&TBL=EN_NEWS&RCN=EN_RCN_ID:20466&CALLER=EN_NEWS

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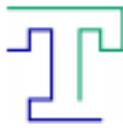
The full text of the CORDIS News interview with Dr. Renzo Tomellini, head of Nanosciences and Nanotechnologies at the European Commission, is shown in the Appendices section of this report (Appendix 7.2).



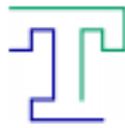
4 Key Players in Risk Assessment of Nanotechnology

Alphabetical list of Authors from Studies presented in Chapter 3:

- **Arata, Manuela**
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- **Arnall, Alexander Huw**
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- **Baumgartner, Walter**
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- **Borm, Paul J.A.**
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- **Chen, H. H.**
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- **Colvin, Vicki**
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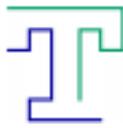


5 Conclusions

The debate about potential benefits and risks of nanotechnology is ongoing. Although hard data on "nanopollution" and toxicity of synthetic nanomaterials is emerging, it is widely accepted that there is a lack of knowledge regarding the environmental consequences of materials containing nano-scale ingredients (e.g. nanoparticles, nanotubes, fullerenes). These types of studies are of paramount importance as a basis for quantitative risk assessment strategies and for future regulations and exposure recommendations. Importantly, more conclusive data on the environmental effects of synthetic nanomaterials will be a key in building the public's trust for nanotechnology.

6 Acknowledgements

The authors are grateful for invaluable comments, suggestions and contributions from Prof. Dr. Hans-Joachim Güntherodt, University of Basel, Prof. Dr. Mihail C. Roco, National Science Foundation USA and Dr. Renzo Tomellini, European Commission, Brussels.



7 Appendices

7.1 Interview with Dr. Renzo Tomellini

Supporting responsible nanotechnology research will benefit Europe's citizens, says head of unit

The Commission's role is not to promote nanotechnology per se, but to develop knowledge of nanosciences and nanotechnologies in order to help and support Europe's citizens. The Commission is doing this by supporting research into both the uses of nanotechnologies, and the possible side effects, said Renzo Tomellini, head of unit for nanosciences and nanotechnologies in the European Commission, in an interview with CORDIS News.

The use of materials at the 'nano' scale is not new. Nanoparticles were used by the Romans to make glasses, and during the Renaissance period to make ceramic. However, although some elements were used in the past, it is the understanding of nanotechnology and how it can be used which is new. This development has led to an increased interest in the subject. Mr Tomellini believes a growth in scientific knowledge and capacity as well as the confidence of scientists led to the higher profile of nanotechnology, coupled with the launch of a very visible nanotechnology initiative in 2001 by then US President Bill Clinton.

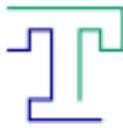
'Nanotechnology became in fashion. Of course, as with everything in fashion, there are expectations and hopes, but also sometimes polemics and fears, and now nanotechnology has become a bit of a show piece.'

The potential of nanotechnology and this increased interest was mirrored by the Commission's framework programmes. Funding for nanotechnology projects began under the Fourth Framework Programme (FP4), which ran from 1994 to 1998. Funding continued under FP5, and was increased significantly when 'nanotechnologies and nanosciences, knowledge-based multifunctional materials and new production processes and devices' became a priority under FP6, and was consequently allocated 1.3 billion euro for projects funded between 2003 and 2006.

The rise in interest in nanotechnology is also evidenced by the response that the Commission received to its first FP6 call for proposals. Almost 1,000 proposals were submitted following the joint call for nanotechnology and material production processes and devices (priority 3). The total funding requested in these proposals was 7.5 billion euro. The budget for this first call is, however, 0.4 billion euro. Proposals ranged from quantum mechanics to applications such as material science and devices for health care. Evaluation of the proposals using the new instruments (which account for around half of those received) will finish in July, while evaluation of the proposals outlining specific targeted research projects has just been completed.

A conference in the European Parliament on 11 June highlighted many concerns with regard to nanotechnology, which Mr Tomellini believes illustrated the need for science-based information and the desire to be informed: 'We intend providing such information, on the one hand by supporting responsible research projects, and on the other hand by funding appropriate studies.'

Mr Tomellini emphasised that the fears of perceived (even if sometimes unrealistic) risks should be taken into account, and highlighted justification, in addition to concern for



Europe's citizens, for carrying out such research. '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. The citizens have had to pay - for health care, etc.,' said Mr Tomellini.

'Our scope is not to support nanotechnology in itself [...]. Our scope is to help people, to serve people, to improve the quality of life for people, to improve industrial competitiveness, to protect or improve the environment, to support European policies [...]. Nanotechnology is a tool, an approach,' said Mr Tomellini. 'The interesting thing is that nanotechnology seems to be a very powerful approach to achieving these goals.'

Every project selected for funding by the Commission will also contain, where appropriate, safety, ethical, metrology and educational aspects. 'This is the advantage of integrated projects,' explained Mr Tomellini. 'They integrate research with everything which is around research, and that allows a future technology to be developed and introduced in the market and society.'

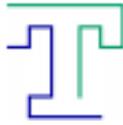
For this reason, speaking always in a personal capacity, Mr Tomellini spoke of his belief that a moratorium on some 'nano' research, as requested on 11 June by some speakers, would 'cause us to lose positive momentum, impoverish our knowledge and ability to understand and decide, and waste precious opportunities to develop useful technologies.'

'We have to do things together, to do simultaneous engineering: expanding knowledge of possible new technologies and the associated risks - if there are any. A linear approach is no longer successful, even in industry. We cannot first study nano-powders and then see whether they are dangerous and take the measures to repair disasters that have already happened. This is not responsible. We cannot, however, stop studying before we know in depth the basic principles, and which materials, products or services we can create. We have to carry out studies simultaneously and to be responsible,' said Mr Tomellini.

Mr Tomellini believes that books and articles have contributed to fears about nanotechnology. Some have combined invisibility, movement and the possibility of reproducing and learning, to create hypothetical 'nano-robots'. 'As presented, these fears are not realistic, are beyond science fiction, and have little or nothing to do with nanotechnology,' said Mr Tomellini. 'Knowledge (and research) dispense with unjustified fears. Moreover, we have to distinguish between science and its possible applications. For example, I cannot see any problems in improving the optical properties of glasses, the mechanical properties of a material or the functionality of a surface.'

Announcements regarding the use of nanotechnology by the military have perhaps fuelled this fear, according to Mr Tomellini: 'Probably the tragedy of 11 September complicated the life of nanotechnology a bit,' he said. 'Security has become a priority, and nanotechnology, being a powerful tool, is being seized also by the military.'

The scientific community is working hard to acquire new knowledge in the 'nano' dimension. Initiatives have also been launched to raise awareness of nanotechnology and the reality behind the misconceptions. A documentary video has been produced and is available to stakeholders, museums, educational institutions and the media across Europe. A second video, aimed as an introduction to nanotechnology for a younger audience, will be ready soon.



7.2 7th ETH Conference on Combustion Generated Particles

Book of Abstracts, Content Section

7th ETH Conference on Combustion Generated Particles

Zurich, 18th - 20st August 2003

Book of ABSTRACTS

Status: 8.July 2003

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