Submissions Scientific Hearing on Nanotechnology

Submission: 1 Withheld upon request of the author

Submission: 2

name Dr. Harald Tillmanns

Individual

publishing Yes

Comments In the past I send already several contributions on the discussion of carbon respectively graphite bulk materials and the differences in structure of bulk C-substances and the significant different structure e.g. of nano-scalec C-materials like fullerens / nanotubes / graphene / graphene foam. New investogations on further studies on the structure of the different types of C-materials showed that this can be proved be.g.by x-ray analysis: - graphite is a stack of more or less perfect planare layers where the the orientation in the direction La = Lb are the same and may only differ in there extention. The orientions in Lc is defined by the naumber of stacked layers and an average interlayer distance of < 3,44 Angstroem. Which can be characterised by x-ray diffraction measurement. - carbon or amorphous respectively isotropc oriented carbons can be described by the an average interlayer distance greater than 3,44 Angstreom. The perfect isotropic C-structure is called diamond. therefore all natural respectively synthetic carbons respectively graphites materials are located somewhere between a single cristall graphite structure and a diamond structure and have defined three dimensial orientation different from nanoscaled C-substances . The structure of this types of so called bulk carbons / graphite differ clearly and measureable structural keydata from so-called nanoscaled C substances / molecules . Here a few e.g. - fullerene are isotropic ball like structure of of single or multilyer structure with equal structure orientation La=Lb=Lc - nanotubes are anisotropic structure of concentric tubes with an orientation of La=Lc and a different orientation in Lb varying in the extention. - graphene and graphene foam exist of mono layer element with LA=Lb and Lc=1 For all other types of nanoscale C-substances comparable differentions in the orientions can be described and prooved by x-ray measurement. Considering the differences which can be detected by X-ray measurement leads clearly to the result that all types of nanoscaled C-substances can and have to be evaluated as independed, individual substance. Newer results show that typical structural characteristics of nanoscled C-substances are found in low concertrations in carbon black. Further structural investigtions (e.g. X-ray have to prove where nanoscaled C-substance may grouped with carbon black.x-ray. A furher indication that nanoscaled C substances have to separated in the grouping from graphite respectively carbon are. - bulk type carbon and graphite substances are formed in a liquid or solid phase thermal decomposition process and can be mechanically reduced in grain size down to min. 1 mµ - nanoscaled C substances are formed by a nucleation process in respectively out of the gas or vapor phase or on a catalytically initiated nucleation process forming defined moleculare structure "molecules" of similar three dimensional satom orientation (e.g. single walled and multiwalled nanotubes and different molecular weights in arrange of < 1nm upt to max 500 nm. Larger sized are agglomerated initally formed nanoscaled particles. Therefore based on x-ray struced studies a grouping of defined nanoscaled C-substances with bulk type carbon respectively graphite is not based on natural science base and REACh related definitions of an acceptable sameness of both types of C mterils and have to be evaluated separately as individuals. Whther a comparable differentions in structural / molecular characterisation for other materials e.g. TIO2 is applicable has to be investigated

See attachment pdf

Submission: 3

Organisation Danish Agriculture and Food Council

Type NGO

publishing Yes

Comments The Danish Agricultural and Food Council believes it is necessary that the legislation has a thorough focus on ensuring the safety of products produced with different kinds of nanotechnologies. The Danish Agricultural and Food Council do, however, strongly believe that the use of nanotechnologies must be regulated in the relevant sectors such as labour environment, food legislation or health rather than in a specific horisontal regulation on nanotechnology. It is, however, essential that the regulations has a strong focus on the different safety issues in the very broad range of nanotechnologies in regard to different characteristics of nanoparticles compared to larger particles. As the specific nanotechnologies are very different it could be more appropriate to address the specific characteristics of different products rather than trying to create a common approach to not necessarily comparable nanotechnologies. Each single product should therefore be assessed from case to case in relation to the specific impact in relation to the environment, public health, nutrition etcetera. It seems neither possible nor relevant to have a specific horizontal regulation regarding nanotechnologies. At the same time it is important to focus on and recognise the public scepticism in relation to nanotechnologies. Finally the Danish Agricultural and Food Council find it is important to fund research both in relation to developing new nanoproducts and in risk assessment.

Submission: 4

Organisation Demeter-Verband

Type NGO

publishing Yes

Comments The Demeter Association Switzerland recommends an extensive investigation in the consequences of using products made with nanotechnology for agriculture, food production and food processing and package materials, as well as for surfacing on products, for textiles, cosmetics and personal care products, polishing products and other consumer products. The investigation must focus on the impact of nanotechnology processes and products on the environment in general, security of employment, farming, and health aspects for all living organisms including humans. The Demeter International standards for Biodynamic agriculture and food processing have banned the use of nanotechnology and products containing nanotechnology ingredients to ensure the safety and health of the environment and human beings. Section 5.1.2.5 of the Demeter International processing standards, and Section 6 of the production standards state that Demeter International adopts the precautionary principle in the implementation of nanotechnology, and therefore excludes it from all usage in Biodynamic agriculture, and from all Demeter certified products. 5 year moratorium In order to maximise focus on the need for a more risk oriented scientific investigation into the effects of nanotechnology on the environment and consumers, we call for a 5 year moratorium on production and marketing of products with nanotechnology elements. It should include all products with a potential for polluting soil, water, manure, plants, animals, food and human beings. We recommend the EU work out a strategic plan to initiate the scientific trials necessary to investigate the relationship between nanotechnology and health.

Submission: 5

Organisation Colipa

Type Trade union

publishing Yes

Comments A consortium of supplier and user companies led by Colipa has recently submitted physical/chemical and safety data on TiO2 as a nanomaterial in cosmetic formulations to the Scientific Committee on Consumer Safety (SCCS). The Committee requested especially data on the particle size of TiO2 in real-life cosmetic (sunscreen) formulations. Extensive studies performed with Transmission Electron Microscopy (TEM) demonstrated that the nanomaterial is present in cosmetic formulations as agglomerates and aggregates, but not as isolated particles. These data are important for exposure considerations and give support to the findings of in vitro and in vivo tests that TiO2 does not penetrate intact skin. Obviously these data are covering only a part of the overall exposure assessment the SCENIHR has to complete, but may nevertheless be helpful for the work of the Committee. The consortium would welcome SCENIHR using these data for their assessment. In case they cannot be obtained from the SCCS, Colipa would be happy to forward the reports to the SCENIHR secretariat. Furthermore this submission also used the data generated under the EU sponsored Nanoderm project. The final report of this project is publicly available under this link: http://www.uni-leipzig.de/~nanoderm/Downloads/downloads.html

Submissions 6 and 7 : withheld upon request of the author

Submission: 8

Organisation Organic Denmark

Type NGO

publishing Yes

Comments Organic Denmark (Økologisk Landsforening) recommend a thorough assessment of the consequences of the use of nanotechnology in agriculture, food production and food processing and package material as well as for surface cover, textiles, cosmetics and personal care products, polishing products and other consumer products. The assessments must focus on the impact of nanoparticles and products on the environment in general, worker health, farming and the health of humans and other living organisms. 5 year moratorium In order to allow a scientific risk assessment of nanoparticles and technology in relation to the environment and consumers we recommend a 5 year moratorium for production and marketing of agricultural and food products where nanotechnology has been used in direct contact with food, feed, the environment or humans. Ideally, the moratorium should include all products with a potential risk of polluting soil, water, manure, plants, animals, food and human beings. The moratorium will allow the the EU Commision to develop a strategic plan for the necessary scientific assesment of health effects from the use of nanotechnology; to adopt necessary limitations and regulations using both scientific knowledge and the precautionary principle, and to develop and disseminate information on possible labeling requirements. As with genetically modified organisms, a moratorium gave the memberstates time to prepare for these crops and products, and find agreement on regulations.

Submission: 9

Organisation MEDITERRANEAN INFORMATION OFFICE FOR ENVIRONMENT, CULTURE AND SUSTAINABLE DEVELOPMENT (MIO-ECSDE)

Type NGO

publishing Yes

Comments Clearly, the rapid growth of nanotechnology applications has by far outpaced the knowledge about associated safety and health risks. The many uncertainties regarding the potential environmental and health effects and the diversity of engineered nanomaterials represent major challenges for a responsible manufacturing and use of these substances. Much of the research undertaken so far, raise more questions than answers. A complete, valid, scientifically sound quantitative, evidence-based risk assessment is needed in order to conduct risk evaluation and risk management. Some critical nanotechnology risk assessment topic areas which have not been covered in the opinions from the relevant EU Risk Assessment Committees and Bodies are the following: • Determination of key factors that influence the dispersion, accumulation, and entry of nanomaterials into the workplace and the environment • Determination of how possible exposures differ by work processes As the applications of industrial nanoparticles are being developed, the concerns on human and environmental health are increasing. According to current scientific knowledge the main potential risks that could emerge from the use of nanomaterials in the future are potential health impacts to biological organisms through inhalation, ingestion, and dermal penetration. Some of the main risks include oxidative stress, cell apoptosis and development of cancer (e.g lung cancer, gill injury) [1-4], brain damage [5], cardiovascular diseases [6-7], and other toxic effects [8-10]. According to MIO-ECSDE's view the key issues to be discussed at the hearing are: ?- The major risks that nanotechnologies pose to the environment and human health. - The most important actions that might be taken by the European community to reduce risks, which are likely to emerge in the short-term, medium term or long-term. The implications in the EU neighboring countries should not be undermined.

References 1. Park EJ, Yi J, Chung KH, Ryu DY, Choi J, Park. K Oxidative stress and apoptosis induced by titanium dioxide nanoparticles in cultured BEAS-2B cells. Toxicology Letters, 2008, 180: 222–229. 2. Lin W, Huang Y, Zhou XD, Ma Y. In vitro toxicity of silica nanoparticles in human lung cancer cells. Toxicology and Applied Pharmacology, 2006, 217: 252–259. 3. Tedesco S, DoyleH, Redmond G, Sheehan D. Gold nanoparticles and oxidative stress in Mytilus edulis. Marine Environmental Research, 2008, 66: 131–133. 4. Federici G, Shaw BJ, Handy RD. Toxicity of titanium dioxide nanoparticles to rainbow trout (Oncorhynchus mykiss): Gill injury, oxidative stress, and other physiological effects. Aquatic Toxicology, 2007, 84: 415–430. 5. Rahman MF, Wang J, Patterson TA, Saini UT, Robinson BL, Newport GD, Murdockc RC, Schlager JJ, Hussainc SM, Ali SF. Expression of genes related to oxidative stress in the mouse brain after exposure to silver-25 nanoparticles. Toxicology Letters, 2009, 187: 15–21. 6. Oesterling E, Chopra N, GavalasV, Arzuaga X, Jin Lim E, Sultana R, Butterfield DA, Bachas L, Hennig B. Alumina nanoparticles induce expression of endothelial cell adhesion molecules. Toxicology Letters, 2008, 178: 160–166. 7. Helfenstein M, Miragoli M, Rohr S, M?ller L, Wick P, Mohr M, Gehr P, Rothen-Rutishauser B. Effects of combustion-derived ultrafine particles and manufactured nanoparticles on heart cells in vitro. Toxicology, 2008, 253: 70–78. 8. K?hnel D, Busch W, Mei?ner T, Springer A, Potthoff A,

Submission: 10

Organisation Institute for Sustainable Development

Type Private non-profit institute for research & development

publishing Yes

Comments Integrated evaluation of risks and benefits for each specific nanoproduct from sustainable development viewpoint (economic, societal, environmental incl. health) during the whole life cycle of specific nanoproduct. Special attention to the use in food, cosmetics and household products. Evaluation of sustainability of supporting materials and technologies (those enabling the use of nanotechnologies and/or nanoproducts). Development of methodologies for evaluating short- and long-term effects of nanoparticles (nanoproducts, nanotechnologies) on human health, including vulnerable populations (children, pregnant women, elderly people). Development of methods for evaluation of the impacts of large-scale applications of nanoparticles/nanoproducts on the environment and human health. Impact of nanoparticles on soil and soil biota.

Submission: 11

Organisation Foreningen for Biodynamisk Jordbrug i Danmark (The Danish Biodynamic Association)

Type NGO

publishing Yes

Comments The Danish Biodynamic Association (Foreningen for Biodynamisk Jordbrug i Danmark) recommends an extensive investigation in the consequences of using products made with nanotechnology for agriculture, food production and food processing and package materials, as well as for surfacing on products, for textiles, cosmetics and personal care products, polishing products and other consumer products. The investigation must focus on the impact of nanotechnology processes and products on the environment in general, security of employment, farming, and health aspects for all living organisms including humans. The Demeter International standards for Biodynamic agriculture and food processing have banned the use of nanotechnology and products containing nanotechnology ingredients to ensure the safety and health of the environment and human beings. Section 5.1.2.5 of the Demeter International processing standards, and Section 6 of the production standards state that Demeter International adopts the precautionary principle in the implementation of nanotechnology, and therefore excludes it from all usage in Biodynamic agriculture, and from all Demeter certified products. 5 year moratorium In order to maximise focus on the need for a more risk oriented scientific investigation into the effects of nanotechnology on the environment and consumers, we call for a 5 year moratorium on production and marketing of products with nanotechnology elements. It should include all products with a potential for polluting soil, water, manure, plants, animals, food and human beings. We recommend the EU work out a strategic plan to initiate the scientific trials necessary to investigate the relationship between nanotechnology and health.

Submission 12 : withheld upon request of the author

Submission: 13

Organisation United States Government

Type Public authority

publishing Yes

Comments COMMENTS OF UNITED STATES GOVERNMENT ON PRINCIPLES FOR NANOTECHNOLOGY ENVIRONMENTAL, HEALTH, AND SAFETY OVERSIGHT Response To European Commission Directorate-General for Health and Consumers Public Consultation on Risk Assessment of Nanomaterials The United States Government is pleased to provide the following comments to the Health and Consumers Directorate-General of the European Commission as it prepares for the September 10, 2009 hearing on risk assessment of nanomaterials. We would be pleased to provide further comments, and possibly testimony, as the issues under discussion continue to be defined. In 2007 the United States White House Office of Science and Technology Policy (OSTP) and the Council on Environmental Quality (CEQ) led a multi-agency consensus-based process to develop a set of principles to guide the development and implementation of policies for nanotechnology environmental, health and safety oversight across the United States Government. This document may be found at: http://www.ostp.gov/galleries/default-file/Nano%20EHS%20Principles%20Memo_OSTP-CEQ_FINAL.pdf The United States Government commends to European agencies the following principles as well as they develop policies for environmental, health, and safety oversight related to nanotechnology: Risk: While basic features of the health and ecological risk assessment paradigms remain relevant to nanomaterials, careful systematic evaluation of the potential lifecycle hazards of nanomaterials is warranted. Depending on the availability of data, both quantitative and qualitative characterizations of risks may inform decision-making. However, given the current limited information available on most manufactured nanomaterials, a key focus of risk assessment-related research must be to identify where key data gaps exist with respect to selected applications of nanomaterials. As these gaps are being filled, information on workplace practices, emissions, use patterns, and the like, together with preliminary information on nanomaterial properties under specific conditions, is being collected in order to develop best practices for limiting exposure and/or mitigating hazards. International Cooperative Efforts: International cooperation can help promote compatibility in the regulation of nanotechnology. The U.S. strongly supports cooperative efforts in international fora such as the OECD Working Party on Nanotechnology and the OECD Working Party on Manufactured Nanomaterials, as well as organizations developing international standards, as valuable opportunities for cooperating in health and safety-related research and the development of harmonized test guidelines and measures. Such cooperation facilitates collaborative testing initiatives, advancement of exposure mitigation approaches, and information exchange and cooperation on voluntary and regulatory mechanisms and on development of policy. These in turn help ensure that the policy development process takes into consideration the inputs of all stakeholders and that the end results are globally relevant. These efforts will allow all parties to contribute to, and take advantage of, risk assessment and risk management approaches across the international community. Statutory Authorities: We believe that existing statutory authorities in the U.S. are generally adequate to address oversight of nanotechnology and its applications and as with any developing area, as new information becomes available we will adapt or develop additional oversight approaches as necessary. The United States Government believes in the value of international cooperation, collaboration, and coordination, and welcomes the opportunity to work with European authorities with regard to oversight approaches relating to nanotechnology and its applications.

Submission 14 : withheld upon request of the author

Submission: 15

Organisation Nanotechnology Industries Association

Type Business

publishing Yes

Comments We agree with SCENIHR that '[t]he hypothesis [...]', (p 53) the case-by-case approach recommended (p 56), & the finding that '[f]or (partially) soluble [...]' (p 7). It is important to distinguish the linearly particle size-dependent increase of surface area from the unique properties that are observable below a primary particle size of approximately 100nm only. More research is needed to characterise the transport properties of primary particles in biological systems, determine if agglomerates or aggregates can revert to primary particles in biological systems, & to shed light on the suggestion that '[f]or low solubility [...]' (p 7). We do not support the introduction of an additional parameter to uniquely describe nanoscale properties by 'extending the [...]' (p 7); it represents a direct dependence on particle size & contradicts the conclusion that '[t]he hypothesis [...]'' (p 53). While we support the notion of a minimum surface area, below which no material shall be considered to be a nanomaterial, we do not support the definition of NMs on one physico-chemical property alone. The cosmetic industry has worked with the EC on the definition laid down in the Cosmetics regulation & is preparing notification of NMs to the EC along the lines of the legal definition for regulatory compliance purposes; discussion of "definition" should acknowledge the existence of this regulatory development. We don't agree with the questioning of the terminology 'nanomaterial' (see '[d]epending on the [...]' (p 7)), cf. ISO TS 27687. We agree that many of the existing NMs in commercial use have been extensively studied & have been found to present no significant hazard. Significant progress on reference materials (p 7) is being achieved by the OECD WPMN [2,3]; industry & regulators are committed to making resources & funding available, & a repository of these & other reference NMs is being established by the JRC. Further coordinated research is required to investigate the transport & fate of primary NPs in biological systems, & to achieve the necessary verification of speculation that suggest 'from the lung [...]' (p 8). The existing history of NMs needs to be reviewed. NMs are created in large volumes in nature (e.g. by volcanoes). How life forms have evolved to handle NMs must be better understood. We agree that further coordinated research is required to investigate the effects of primary NPs on cardiovascular systems (see'[b]ased on the observation [...] (p 8)); and the mechanism of tox. effects of NMs (in particular primary NPs) on biological systems; without conclusive determination of the transport & fate of primary NPs, the detection of ROS generation in hazard studies remains speculative. SCENIHR summarises inconclusive evidence by stating that 'there is some evidence [...]' (p 9), but all studies of mechanism of tox. effects must be conducted using exposure-relevant experimental protocols & tests. Walker et al. concluded that 'the specific composition of an in vitro & in vivo test system will likely play a huge role in how a [NM] interacts with a cell, or other biological target. […] Depending on the experimental conditions used, […], what was "tested" may often bear little resemblance to the material as it exists in the real world or in a different test system.' [1] The OECDC WPMN SG8 finds that '[e]ven in the absence of specific exposure limits or guidelines for engineered [NPs], exposure measurements can still be used to determine the need for & effectiveness of engineering controls or work practices.' [2,3] We agree that more coordinated research is required to improve the understanding of derivatisation of NMs in the environment, & welcome the conclusion on the hazard assessment of CNTs: '[w]hether such nanotube [...]' (p 9). Others found that'[a]fter 24 months, [...] MWCNT [...] did not induce mesothelioma [...]. The incidence of tumors other than mesothelioma was not significantly increased across the groups'.[5]

References [1] Walker, N. J. and Bucher, J. R., 'A 21st century paradigm for evaluating the health hazards of nanoscale materials?' Toxicol Sciences, in press 2009. [2] We wish to note that, as part of the OECD Sponsorship Programme, the NIA is leading a consortium, which develops detection and tracking equipment (using isotope tracking) and tests the ecotoxicology and environmental fate of two of the agreed 14 nanomaterials (i.e. ZnO and CeO2) in detail. It is anticipated that prototypes of detectors will be developed that allow the isotope tracking of these and other suitable particles in different media. We agree with SCENIHR that '[t]here is a need to further establish reliable and standardised measurement

techniques, to develop measurement strategies, and to further implement screening/monitoring of nanoscale particles in sensitive work areas.' [3] For more information on the OECD Sponsorship Programme of Manufactured Nanomaterials, please follow this link: http://www.nanotechia.org/news/global/oecd-launches-sponsorship-programme-to-test-a-repr [4] Poland C, et al., 'Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study'. Nat Nanotechnol 2008; 3:423-8. [5] Muller, J. et al., 'Absence of carcinogenic response to multi-wall carbon nanotubes in a 2-year bioassay in the peritoneal cavity of the rat.' Toxicol Sciences, in press 2009. [6] summary: In summary, we recommend the following issues to be considered for further focus by the Scientific Committees: • distinction, description and determination of unique nanoscale effects and properties (as opposed to those that are extrapolations from a larger size, such as surface area dependent reactivity) • support of technology- and science-based terminologies and definitions agreed by international fora • coordinated research in the following area needs to be advanced and the resulting findings reviewed: o release and fate, and exposures of nanomaterials within the environment o transport and fate of primary nanoparticles in biological systems o mechanism of toxicological effects caused by nanomaterials in biological systems o establishment of reliable and standardised measurement techniques, [...] and implementation of screening/monitoring of nanoscale particles o improvement of the understanding of derivatisation and alteration of nanomaterials in the environment.

Submission: 16

name Dirk van Aken

Individual

publishing Yes

Comments [Topics that have not been covered in the opinions from the relevant EU Risk Assessment Committees and Bodies] In general, the recent opinions of the SCCP (2007), SCENIHR (January 2009) and EFSA (February 2009) are quite complete in their analysis of necessary scientific knowledge. Our first concern, however, is that we are not even certain in which products nanomaterials are used. For example, EFSA has recommended monitoring current and future commercial applications of ENMs in food and feed; this is very difficult for market surveillance authorities as long as products are not identifiable and methods for routine analysis of nano-ingredients in the lab are not available. A notification duty or obligatory registration of products containing nanomaterials could solve this problem and the REACH regulation offers a basis. Much is still uncertain about the route(s) by which nanoparticles may enter the human body. In particular, knowledge about oral uptake is scarce, whereas this will be an important route for food (and contact materials). Assessment of exposure to substances emitted by or migrating from consumer products is a challenge in any case, and it is even more difficult when nanomaterials are involved. Existing migration tests need to be validated for nanomaterials. Exposure models and tools such as ConsExpo could help in analysing exposure, but many data required as input in these models are lacking for nanomaterials, and questions about dose metrics should be resolved. [The main potential risks -according to current scientific knowledge- that could emerge from the use of nanomaterials in the future] Research so far seems to indicate that the long-term effects of exposure to nanomaterials are the major concern. For consumer products, important questions to be addressed are: to what extent may nanomaterials be released from consumer products under foreseeable use conditions; what are the relevant exposure routes; what effects can be expected upon exposure, in particular on the long term (cardiovascular system, carcinogenic, mutagenic, reprotoxic effects)? [Issues to be discussed at the hearing including provision of background information and comments on those issues] Are there any specific examples of nanomaterials for which a thorough risk assessment is already possible? What types of nanomaterials should be given priority? (A logical choice seems to be: engineered, insoluble, persistent nanoparticles that are already in use or will be used in the near future). How can we speed up research aimed at validating existing test methods to nanoparticles? How can we gather and share good and reliable exposure data? How should we evaluate exposure of consumers in a consistent and worldwide-accepted way? What analytical and measuring methods and equipment for concentration and other

characteristics of nanoparticles are already available, which ones should be developed? How can the effects of nanoparticles in the body be studied efficiently and what is the influence of particle characteristics on absorption, distribution, metabolism and excretion? How should we investigate the effects of selected nanoparticles on cells, organs and organisms, and the dose-effect relationships (determine threshold values, if any). Pending the results of OECD cooperation and FP7 projects, screening tests are important to detect clearly undesirable effects.

Submission: 17

Organisation Foundation Animalfree Research

Type NGO

publishing Yes

Comments The Foundation Animalfree Research acknowledges the opinions on safety-related aspects of nanotechnology from the relevant EU Risk Assessment Committees and Bodies and welcomes the present opportunity to identify issues for the EU Commission's Scientific Hearing on the safety of nanomaterials. In recognition of the importance of reliable and reproducible test methods to determine the safety of nanomaterials and in recognition of the main goal of the REACH Regulation 1907/2006 to promote alternative methods (Article 1(1)), the promotion, development and validation of non-animal test methods and the development of non-animal testing strategies for the safety testing of nanomaterials is an important issue to be discussed during the Scientific Hearing. Animalfree Research agrees with SCENIHR (2009) that the methodology for both exposure estimations and hazard identification needs to be further developed, validated and standardised. However, we disagree with SCENIHR that in vitro assays may be useful mainly for screening and the evaluation of specific mechanistic pathways. We would like to note that the reports cited by SCENIHR in this context (1, 2) apparently do not cover those non-animal test methods making use of the most recent of advances in biotechnology to evaluate the effects of nanomaterials. As regards the safety testing of nanomaterials, where validated test methods or testing strategies so far do not exist, scientific and political efforts should set out to develop non-animal test methods and a non-animal testing strategy from the beginning instead of continuing to rely on outdated, distressful animal experiments. The US National Research Council has spelled out a paradigm change from in vivo to in vitro testing strategies as a vision for the 21st century (3): "Change often involves a pivotal event that builds on previous history and opens the door to a new era… Toxicity testing is approaching such a scientific pivot point. It is poised to take advantage of the revolutions in biology and biotechnology. Advances in toxicogenomics, bioinformatics, systems biology, epigenetics, and computational toxicology could transform toxicity testing from a system based on whole-animal testing to one founded primarily on in vitro methods that evaluate changes in biologic processes using cells, cell lines, or cellular components, preferably of human origin." We agree with SCENIHR that to be applicable in risk assessment, assays need to be validated and their relevance for in vivo hazard identification demonstrated. Likewise, we confirm SCENIHR's observation that also in vivo assays have not yet been validated. However, we disagree with SCENIHR that the experience gained in the testing of chemicals with in vivo assays indicates that they can be used for the detection of some potential hazards of nanomaterials. Experience with a test method does not render its scientific validation unnecessary: "Learning from experience may be nothing more than learning to make the same mistakes with increasing confidence", (4). Experience can only supplement validation as a prerequisite for the sound application of any test method. Moreover, experience is not an issue distinguishing in vivo from in vitro tests. Experts in the area of alternative methods, scientists from ECVAM and national authorities dedicated to the replacement of animal experiments such as ZEBET in Germany, should be involved in the task to develop non-animal testing strategies for nanomaterial safety testing. We would welcome the opportunity to discuss these issues with the EU Commission so that the research needs identified by SCENIHR will be met, to make available validated in vitro assays and to include quantitative structure activity relationship (QSAR) assessments in the testing strategy. The development of non-animal testing strategies to study the potential harmful effects of nanomaterials serves human health and environmental safety as well as economic interests (5).

References (1) Warheit DB, Hoke RA, Finlay C, Donner EM, Reed KL, Sayes CM (2007). Development of a base set of toxicity tests using ultrafine TiO2 particles as a component of nanoparticle risk assessment. Toxicol Lett 2007; 171:99-110. (2) Sayes CM, Reed KL, Warheit DB (2007). Assessing toxicity of fine and nanoparticles: Comparing in vitro measurements to in vivo pulmonary toxicity profiles. Toxicol Sci 97,163-80. (3) CTTAEA and NRC (2007). Committee on Toxicity Testing and Assessment of Environmental Agents, US National Research Council. Toxicity Testing in the 21st Century: A Vision and a Strategy. National Academics Press, 216 pp. http://www.nap.edu/catalog.php?record_id=11970#toc . (4) (Petr Skrabanek and James McCormick, Follies and Fallacies in Medicine, Tarragon Press, Glasgow, 1989). (5) Sauer UG (2009). Animal and non-animal experiments in nanotechnology – the results of a critical literature survey. ALTEX 26/2, 109-134.

Submission 18 : withheld upon request of the author

Submission: 19

Organisation Department of Toxicology and Chemical Management, IBM Corporation

Type Business

publishing Yes

Comments The Department of Toxicology and Chemical Management at IBM Corporation is contributing the following comments to address one of the expected outcomes of the upcoming European Commission scientific hearing on nanotechnology, i.e., the identification of possible topics which have not been covered adequately in the opinions from the relevant EU Risk Assessment Committees and Bodies. The development and manufacture of engineered nanoparticles is an important output of nanotechnology because at the nanoscale, particles can have unique properties that enable novel and useful applications. Nanotechnology encompasses more than just engineered nanoparticles, however. Nanotechnology today is an emerging set of tools, techniques, and unique applications being used to create functional devices and systems that may not contain discrete engineered nanoparticles but do contain nanoscale features. For example, the nanoscale junctions of transistors, which are involved in transmitting, processing, and storing information, are created by processes that etch or otherwise modify minute parts of a larger block of material - a silicon wafer. Such nanoscale features, patterned as integral and fixed parts of a much larger object, are distinct from discrete engineered nanoparticles. Therefore, it is critical that the consequential distinction between nanotechnology and engineered nanoparticles on potential environmental and health impacts be further developed in the EC scientific hearing on nanotechnology in order to accurately identify the potential hazards and ensure the responsible and sustainable development of nanotechnology. Intense competition and phenomenal innovations have pushed the current information technology (IT) platforms (the basic hardware and software technology of a computer system that defines how a computer is operated) close to their fundamental physical limits, in which traditional approaches to reduce feature size and increase functionality are becoming prohibitively difficult and expensive. The expanded use of nanotechnology and the potential to incorporate nanomaterials in IT systems allow extension of current conventional IT platforms and enable revolutionary new innovations and technologies beyond current platforms to create new products, services, and economic growth, and new channels of global communication, interaction, and collaboration. In addition to driving technological innovations and performance enhancement, nanotechnology also provides a tremendous opportunity for pollution prevention in IT. The application of nanotechnology can lead to energy and resource conservation and waste minimization in IT manufacturing processes, and highly energy efficient IT products. Although the timing of future applications is dynamic, it is important to emphasize that nanotechnology is not new to IT; the industry has been working successfully and safely at the nanoscale for several decades. While nanotechnology has been critical to the success of the IT industry, its potential is now being developed to revolutionize and transform other technologies and industries to drive economic growth and serve public good. Amid excitement over the potential societal benefits of nanotechnology, there is also a concern that particles that are purposefully manufactured with nanoscale dimensions, i.e.,

engineered nanoparticles, may cause harm to human health and the environment. In addressing the environmental, health, and safety concerns associated with nanotechnology, it is important to understand the relationship and distinction between nanotechnology and engineered nanoparticles, and take into consideration that many tools, techniques, and applications of nanotechnology do not involve the production, use, or release of engineered nanoparticles.

Submission: 20

Organisation European Public Health Alliance

Type NGO

publishing Yes

Comments The European Public Health Alliance (EPHA) is the largest European Platform representing 86 member organisations working in the field of health. EPHA's membership is unique in its diversity and includes patient groups, healthcare professionals, public sector bodies, disease-specific organisations, treatment groups and others. Members include international, European, national, regional and local level organisations throughout Europe. EPHA's mission is to protect and promote public health in Europe. Please see www.epha.org for more information. Adequate and effective regulation of nanomaterials and nanotechnology represents a current need for the health sector. Such regulation is vital to ensure that products containing manufactured nanoparticles are safe and beneficial to consumers and do not lead to new human health and environmental risks. Inadequate funding and the lack of governmental emphasis on the potential human health risks associated with nanotechnology has led to a situation where, despite the lack of testing methods and technology to adequately assess the long-term health impact, there are hundreds of consumer products on the market that either contain nanomaterials or are made using nanotechnology. In light of the mounting evidence highlighting the potential for significant health risks, the European Commission should convene consultations among the relevant regulatory bodies to exchange data and establish an improved approach to assessing and preventing risks. Such an approach would involve a broadening of the regulatory systems in order to address the specific characteristics of nanomaterials. New regulations are required to manage nanomaterials; a 2008 survey showed that industry was failing to undertake adequate risk assessments on a voluntary basis[1]. The European Commission and its advisory committees, including the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and the Scientific Committee on Consumer Products (SCCP), should endeavour to identify the key risks and address the issue of significant knowledge gaps. In its 2006 report[2], the EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) recognised the systemic failure of existing chemicals regulatory frameworks to manage the risks of nanomaterials. A strong precautionary approach to manage nanotechnology is recommendable: -Mandatory safety testing of nanomaterials prior to their inclusion in commercial products- these assessments should be carried out by independent scientific committees. -The EU should establish a mandatory reporting scheme to keep track of the introduction of manufactured nanomaterials into the marketplace. In addition, the EU should establish a public inventory of all current and forthcoming nanomaterials used in products on the market. -Requirements for product labels to indicate the presence of manufactured nanomaterials/particles- in particular those products with which consumers come in direct, close or regular contact such as food, medicines and cosmetics. -Agreement on definitions of nanomaterials and nanotechnologies- the lack of definitions leads to legal uncertainties and can delay the establishment of effective regulation. - Existing European legislation relevant to nanotechnologies should be adapted in order to safeguard public health and safety. - Public participation in decision-making regarding nanotechnology's introduction and in determining priorities for public spending on nanotechnology research and development.

References [1] Siegrist M, Wiek A, Helland A, Kastenholz H (2007). "Risks and nanotechnology: the public is more concerned than experts and industry". Nature 2:67 [2] SCENIHR (2006). "Scientific Committee on Emerging and Newly Identified Health Risks: The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of

nanotechnologies", European Commission

Submission: 21

Organisation Bayer AG

Type Business

publishing Yes

Comments We would like to thank the EU Commission for the opportunity to participate in the public consultation. A/ First we present some general remarks related to the SCENIHR Opinion on "Risk Assessment of Products of Nanotechnologies" published in 2009. 1) Risk assessment can be performed on a case by case basis We agree with the SCENIHR opinion which recognizes that nanomaterials represent a heterogeneous class of materials. A generalisation or general risk assessment is not meaningful. Some nanomaterials may be toxic, others may not; the handling of some nanomaterials may lead to an exposure or not; a case by case ("substance by substance") approach and expert judgement will play an important role. 2) The Technical Guidance Documents are suitable for nanomaterials We believe it is important to emphasise that the Technical Guidance Documents (TGD) are generally likely to be able to identify the potential hazards of nanomaterials. It is likely that modifications related to the phys-chem. characterisation may be necessary. The Risk Assessment methodology in place within the EU is an established process which was used for a whole range of diverse chemical substances, and should be applied to nanomaterials in a first instance to identify on a case by case exercise whether some steps have to be modified. 3) OECD test guidelines are generally appropriate for nanomaterials In general the OECD guidelines are appropriate for investigating the health effects of nanomaterials with the important proviso that additional consideration needs to be given to the physicochemical characteristics of the material tested, including such characteristics in the actual dosing solution. In some cases there will be a need for further modification to the OECD guideline. SCENIHR (2009) confirms that "many of the currently available OECD guidelines for the testing of chemicals are likely to be adequate to detect potential hazards of manufactured nanomaterials as well". The importance of a validation process for testing procedures for nanomaterials is duly noted. 4) Definition SCENIHR proposes an extension of the definition for nanomaterials that is not based on size alone but also on specific surface area. We believe this is premature as the discussion on the appropriate metrics of dose is still open (Pauluhn (2009) Toxicology 259(3):140-8; Sager, Castranova (2009) Particle and Fibre Toxicology 6:15; Warheit et al. (2007) Toxicology 230; 90-104; Warheit et al. (2007) Tox. Sci. 95(1), 270-280). B/ To the questions raised in preparation of the scientific hearing on nanotechnologies, we believe that the following points should be prioritised in the next future: - Due to the large number of publications and ongoing research programs a review should be undertaken for each class of nanomaterials. The review should include first a comprehensive collection of published (eco)-toxicological evidence followed by an evaluation of the relevance of the published studies for a risk assessment. - To refine analytical methods to differentiate between human exposure to natural and man-made airborne nanoparticles - To improve the database on the potential genotox effects of nanoparticles - To further investigate the toxicokinetics of nanoparticles - To further investigate the applicability of newly developed in vitro test systems and, as long as these have not been validated, continue to put more emphasis on in vivo experiments (Donaldson et al., Particle and Fibre Toxicology (2009), 6:13; Sayes et al., J. Nanopart. Res. (2009) 11:421-431; Lanone et al., Particle and Fibre Toxicology (2009), 6:14)

References Pauluhn (2009) Toxicology 259(3):140-8; Sager, Castranova (2009) Particle and Fibre Toxicology 6:15; Warheit et al. (2007) Toxicology 230; 90-104; Warheit et al. (2007) Tox. Sci. 95(1), 270-280 Donaldson et al., Particle and Fibre Toxicology (2009), 6:13; Sayes et al., J. Nanopart. Res. (2009) 11:421-431; Lanone et al., Particle and Fibre Toxicology (2009), 6:14

Submission: 22

Organisation European Environmental Bureau and Friends of the Earth Germany (BUND)

Type NGO

publishing Yes

Comments EEB and BUND (Friends of the Earth Germany) response to the EU Public consultation "Scientific Hearing on Nanotechnology" The issues surrounding the wide spectrum of potential risks and possible benefits associated with the rapid advance of modern nanotechnologies are of high interest for the European Environmental Bureau and BUND from the standpoint of environmental civil society groups. These include the current realities of nanotechnological hazards, their impact vis-a-vis nanotech-risks and benefits, and the consequent repercussions on the public, society and the environment. Our central idea is that the technological risks must be properly and timely communicated to the public (along with the benefits) to ensure the democratic, responsible and safe development of this emerging technology. We also consider that beyond a public hearing on nanotechnologies and related risks, the European Commission should host a public debate on technological innovation as such in the context of sustainability (sustainable production and consumption). Meanwhile, EEB demands that no further market introduction be allowed for products containing manufactured nanomaterials which could lead to exposure of consumers or uncontrolled release in the environment. Such a restriction should be put in place until appropriate impact and safety assessment tests are developed and appropriate nano-specific risk assessment carried out and mandated that provide scientific proof that these materials and products are adequately safe to human health and the environment. Those products already on the market should be should be removed from commercial circulation until proven safe. 1. Identification of any possible topics which have not been covered in the opinions from the relevant EU Risk Assessment Committees and Bodies 1.1 Environmental impacts of nanomaterials have not been addressed in depth 1.2 Lifecycle approach in risk assessment 1.3 Toxicological and exposure data for many emerging nanomaterials are missing 1.4 Assessment of actual human and environmental exposure 1.5 Migration of ENMs 1.6 Next generation of ENMs 1.7 Combined effects of exposure to nanomaterials 1.8 Standard Definition of Nanomaterials still missing 2. Identification of what are, according to current scientific knowledge, the main potential risks that could emerge from the use of nanomaterials in the future 2.1 Human toxicity 2.2 Adverse environmental effects 2.3 Microbial resistance to antibiotics 3. Identification of further issues to be discussed at the hearing 3.1 Gaps in Awareness, Communication, and Training 3.2 Risk assessment tools for new technologies

References Dear DG SANCO team, as the limited character number for the on-line submission to the consultation does not allow us to convey all our comments on the topic of risk and nanotechnologies, we are sending a separate document with our full contribution to be considered for the public hearing. Thank you very much for your understanding. Best regards Dragomira Raeva on behalf of EEB and BUND

Submission: 23

Organisation Institute of Occupational Medicine & the SAFENANO Initiative

Type Independant Research and Consultancy Organisation

publishing Yes

Comments In relation to objective 1 of the call for submissions, the Institute of Occupational Medicine (IOM) & SAFENANO Initiative would like to make 3 recommendations; 1. That more effort is devoted to the question of consumer exposure generally and ingestion exposure specifically in relation to the

presence of nanoparticles in food and in studies to understand the potential of nanoparticles to cross the gut wall and subsequent kinetics; 2. That full Reproductive Toxicity be addressed as part of a hazard assessment for the evaluation of risks associated with nanoparticles; & 3. That much more effort is placed on developing an internationally co-ordinated programme of work to maximise the efficiencies and outputs of research underway and that which will be funded in the future With reference to objective 2 of the call for submissions, IOM/SAFENANO would like to bring into consideration the ongoing appraisal of potential health risks associated with high aspect nanomaterials (HARN). Of particular relevance to this topic is a recently published Defra (UK) report, 'An outline scoping study to determine whether high aspect ratio nanoparticles should raise the same concerns as do asbestos fibres'1. The report identifies many similarities between HARN and asbestos with regard to their physico-chemical properties and toxicological effects, & concludes that there is sufficient evidence to suggest that HARN which have the same characteristics (diameter, length and biopersistance) as pathogenic fibres, such as asbestos, are likely to have similar pathology. In addition, it presents a set of prioritised recommendations for future research, spanning the fields of measurement & characterisation, toxicology studies (both in vitro and in vivo), and exposure & risk assessment. In consideration of the possible health impacts associated with potential translocation of nanoparticles into cells, IOM/SAFENANO would like to put forward evidence presented within the 2009 Defra CELL PEN report. 'CELL PEN: A Study fo identfy the physico-chemcial parameters controlling the capacity of nanoparticles to penetrate cells2 presents an informed commentary and research agenda toward elucidating the importance of translocation in nanoparticle toxicology. In relation to objective 3 of the call for submissions, IOM/SAFENANO would like to put forward for consideration both the HARN and CELL PEN reports (summarised above), and the EMERGNANO report. 'EMERGNANO: A review of completed and near completed environment, health and safety research on nanomaterials and nanotechnology'3 represents the first global review of environmental, health, and safety studies examining the risks of nanotechnology exposure. The review examined more than 670 studies, and appraised more than 250, in the context of the 18 Research Objectives defined by the UK's Nanotechnology Research Coordination Group. IOM/SAFENANO consider that this review is likely to help fame future research studies in terms of effectiveness and need, and thus would like to present it for consideration as evidence for discussion. In consideration of the methodologies for assessing exposure to manufacture Nanomaterials, IOM/SAFENANO would also like to draw attention to the Maynard & Aitken 2007 review, 'Assessing exposure to airborne nanomaterials: Current abilities and future requirements'4. Published in the journal Nanotoxicology, the review presents: 1. a novel classification of engineered nanoparticles into categories based on their physico-chemicals structure, 2. a consideration of the applicability of existing exposure metrics in relation to (1), and 3. suggested key attributes for inclusion in development of new devices for exposure monitoring of nanomaterials. IOM / SAFENANO hope that the evidence outlined above will prove useful in appraisal of the current issues in nanomaterial safety. Signed, R J Aitken, S M Hankin, B L Ross, C L Tran Institute of Occupational Medicine The SAFENANO Initiative

References 1. Tran, CL, Hankin, SM, Ross, B, Aitken, RJ, Jones, AD, Donaldson, K, Stone, V, Tantra, R (2008) 'An outline scoping study to determine whether high aspect ratio nanoparticles (HARN) should raise the same concerns as do asbestos fibres' Report on DEFRA project CB0406 2. Hankin, SM, Tran CL, Ross, B, Donaldson, K, Stone, V, Chaudhry, Q (2008) CELL PEN: A Study fo identfy the physico-chemcial parameters controlling the capacity of nanoparticles to penetrate cells, Report on DEFRA project CB0407 3. Aitken RJ, Hankin SM, Ross B, Tran CL, Stone V, Fernandes TF, Donaldson K, Duffin R, Chaudhry Q, Wilkins TA , Wilkins SA, Levy LS, Rocks SA, Maynard A (2009) 'EMERGNANO: A review of completed and near completed environment, health and safety research on nanomaterials and nanotechnology', Report on DEFRA project CB0409 4. Maynard AD & Aitken RJ (2007), 'Assessing exposure to airborne nanomaterials: Current abilities and future requirements', Nanotoxicology 1 (1): 26-41.

Submission 24 : withheld upon request of the author

Submission: 25

Organisation Evonik Degussa GmbH

Type Business

publishing Yes

Comments Possible topics for the Scientific Committees and potential risks of nanotechnology EVONIK believes that the following subject matters may be priorities for further research activities and of interest for further clarification by the Scientific Committees: 1.Enhanced investigation of the understanding of the behaviour of nanoparticles in the environment 2.Improved understanding of the toxicokinetics of nanoparticles ("Translocation") 3.Improved mechanistic understanding of nanoparticles' potential to alter human DNA 4.To gain a better insight of nanomaterials and particles behaviour in in-vitro systems to refine the existing test methods [1]. 5.Refinement of analytical methods to differentiate between human exposure to natural and man-made nanoparticles 6.Further clarification of the association and mechanistic link to the presence of nanoparticles aerosols and the incidence of cardiovascular disease [2] Specific Comments on the SCENIHR Report, published February 2009 •EVONIK strongly agrees as proposed by SCENIHR that a risk assessment can only be done on a case-by-case basis. Systematic generalisation of the potential hazardous effects of nanomaterials seem inappropriate since it is not possible to conclude that if a specific nanomaterial exhibits effects for certain endpoints, than all nanomaterials have the potential to display the same effects. •To the best of our knowledge OECD and ISO have not come any closer in defining nanospecific properties. EVONIK shares the SCENIHR opinion that nanomaterials are similar to "normal" substances as some nanomaterials may be (eco)toxic, and some may not. •SCENIHR describes potential risks in the report that to our understanding could only occur with specific "nano-objects" including their aggregates and agglomerates based on their small size and should not be generalised to include all nanomaterials. •We believe that the Expert Judgement Matrix, as proposed by SCENIHR, may therefore only be used to suggest one possible approach to conduct a risk assessment. Similarily, risk management measures can only be derived from a thorough case-by-case assessment. •The apparent cardiovascular effects of nanomaterials are emphasised even though the scientific basis for such an opinion may be limited. We believe that such effects are not specific for man-made nanomaterials but a general issue including small ambient particles ("Finedust") phenomena. Statement on Test Guidelines EVONIK would like to direct the attention to the fact that a subgroup of the OECD WPMN (SG4) concluded that the OECD guidelines are in principle appropriate for investigating the health effects of nanomaterials. This is confirmed by SCENIHR: "Many of the currently available OECD guidelines for the testing of chemicals are likely to be adequate to detect potential hazards of manufactured nanomaterials as well (page 23). Definition EVONIK experts are actively involved in the standardisation process at international (ISO), European (CEN), and at national level to further develop and harmonise instruments for nanomaterials testing. SCENIHR proposes a broadening of the definition for nanomaterials that is not based on size alone but also including the following criteria: -substances smaller than about 100 nm and their aggregates and agglomerates and - Specific surface area (by BET) larger than 60 m2/g. In our view an increase in surface area alone does not necessarily correlate with increased hazardous properties. Thus we do not support the view that specific surface area should be a general criterion included in the definition.

References 1. Publications by Iseult Lynch and Kenneth Dawson (NanoInteract project) 2."The potential risks of nanomaterials: a review carried out for ECETOC" Paul JA Borm, David Robbins, Stephan Haubold, Thomas Kuhlbusch, Heinz Fissan, Ken Donaldson, Roel Schins, Vicki Stone, Wolfgang Kreyling, Jurgen Lademann, Jean Krutmann, David Warheit and Eva Oberdorster, Particle and Fibre Toxicology 2006, 3:11 doi:10.1186/1743-8977-3-11; Paul J. Borm: "Future interactions in Particle Toxicology: the role of PFT", Particle and Fibre Toxicology 2008, 5:5 doi:10.1186/1743-8977-5-5; Mossman: "Mechanisms of

action of inhaled fibers, particles and nanoparticles in lung and cardiovascular diseases", Particle and Fibre Toxicology 2007, 4:4 doi:10.1186/1743-8977-4-4 3. Additionally in the OECD workshop on exposure measurement and exposure mitigation from October 2008 it has been concluded that "Measurement techniques and devices are available in principle and have been tested to measure nanoparticles. But standard measurement processes have to be agreed on that are founded on a reliable basis on reference materials and measurement calibration." [OECD Working Party on Manufactured Nanomaterials (WPMN) Workshop on "Exposure Assessment and Exposure Mitigation" 20 October 2008, Frankfurt, Germany, Notes] 4. International Water Association – IWA Report

Submission: 26

Organisation PEROSH and NEW OSH ERA

Type Two networks of primarily government affiliated research centres

publishing Yes

Comments PRIORITIES FOR FUTURE RESEARCH IN NANOTOXICOLOGY Hazard and exposure data on man-made nanoparticles (MNP) are currently inadequate for full and detailed risk assessment of their potential health effects in humans in the working or other environments. Many organisations across the EU and globally are trying to address these knowledge gaps, either by funding or directly carrying out research. Below is a list of topics that PEROSH and NEW OSH ERA from an occupational health point of view consider to be most important in future research projects. Needs for research are primarily within exposure assessment and hazard assessment. Exposure assessment • Greater information on human exposure levels in different scenarios (occupational and consumer) to inform risk assessment; this will require development and validation of measurement strategies and exposure scenarios. • MNP are rapidly scavenged by coarser background particles. Methods that allow determination of MNP attached to coarser background particles should be developed. • Methods and standards for dustiness testing should be developed that are tailored for manufactured nanomaterials; they should include determination of size distribution and agglomeration state of the emitted particles. Such information could be included in material safety data sheets for improved exposure risk assessment. • Besides a need for standardized measurement techniques, measurement strategies and screening/monitoring of MNP in sensitive work areas, there is a need for an approach to analyse the collected data and establish a database. • There is a need for insight into the effectiveness of control measures. Hazard assessment More knowledge is needed of the degree to which occupational exposure to MNP causes health effects and the underlying mechanisms. Specifically, there is a need for: • Rodent experimental studies with emphasis on inhalation exposures for the evaluation of occupational hazard. • Development and systematic inter-laboratory comparison of robust, in vitro / in vivo inhalation toxicity testing approaches, suitable for MNP. It will be impossible to test every type of MNP by inhalation in laboratory animals. A staged approach has been proposed by many scientists, in which MNP are first tested in vitro to select materials that require detailed in vivo analyses. However, robust, in vitro inhalation toxicity testing approaches are not yet available, although inhalation represents the most likely route of exposure in the work-place. • Systematic studies on how particle size, physico-chemical parameters and functionalisation of MNP affect toxicity. This would allow effective comparative hazard assessments to be carried out. • Analysis of the ability of MNP to accumulate to critical levels in certain target organs including both the central and peripheral nervous systems. This would require analysis of the ability of MNP to translocate to the organs, accumulate and have adverse effects. Knowledge of translocation of MNP from lungs or skin to distal organs is insufficient. • Many MNP exist as agglomerates. Knowledge of what happens to these agglomerates when they reach peripheral pulmonary defence systems (i.e. macrophages and inflammatory cells) and biological barriers such as the respiratory surface or gut lining and then cross into the systemic circulation is lacking. This is critical for understanding interactions between MNP and biological systems in terms of their ability to translocate around the body and induce downstream effects. • Studies on the toxicokinetics and toxicodynamics of nanoparticles attached to larger particles. Other relevant research questions • Development of approaches for monitoring and reporting ill-health of workers exposed to MNP. • Development of a risk assessment strategy: decision tree to examine available information and a roadmap

for a structured risk assessment process on which knowledge gaps need to be filled.

Submission: 27

Organisation Friends of the Earth Australia

Type NGO

publishing Yes

Comments Friends of the Earth Australia believes the following areas l have not received adequate attention: 1. The need for precautionary management of nanomaterial risks, with sales of nano-products halted until appropriate nano-specific risk assessment can be developed, validated and mandated. • Particular attention should be paid to a recent review (Aitken 2009) of EHS research on nanomaterials conducted worldwide has identified three nanomaterials as potentially needing a precautionary approach to risk assessment: carbon nanotubes, nanosilver and titanium dioxide. The latter two materials are used in foods or food contact materials. 2. The need to broaden the definition of nanomaterials to encompass particles up to 300nm in size to ensure that this definition is biologically relevant. • A growing numbers of nanotoxicologists recognise that the emerging definition of nanomaterials as measuring 100nm in one dimension or less is inadequate (eg see evidence given to the Nanotechnologies and Food Inquiry held by the UK House of Lords Science and Technology Committee 2009). Leading nanotoxicologists warned the UK House of Lords that the 100nm definition excludes biologically relevant nanoparticles a few hundred nanometres in size, which present similar nanotoxicity risks. 3. The assessment of soluble nanoparticles (eg micelles, nano-liposomes, nano-emulsions and nano-encapsulated active ingredients) as nanoparticles. • Given the poor understanding we have of how the far greater bioavailability, solubility and potency of nano-formulated soluble substances will influence their biological behaviour and potential toxicity, it is essential to subject these nanomaterials to new nanotechnology-specific safety assessments and exposure metrics. 4. The role of aggregation, agglomeration, de-aggregation and de-agglomeration of nanomaterials. • Where toxicity is driven by surface characteristics, the toxic properties of aggregated nanoparticles may be very similar to that of the primary nanoparticles that compose them. Agglomerates have similar structures and surface properties to aggregates and so may also share the toxicity risks associated with the primary nanoparticles that compose them. Additionally, in principle agglomerates can also change shape or come apart (Maynard 2007). If particles do not de-agglomerate, their size could reduce their bioavailability relative to that of their primary nanoparticles (Limbach et al. 2005). However this may not necessarily reduce their toxicity. 5. The public health implications of widespread use of potent antibacterial nanomaterials such as silver. • See our recent detailed report on nano.foe.org.au 6. The public health implications of widespread sales of nanofoods. • We are especially concerned that the public health implications of nanotechnology's use in foods has not been the subject of rigorous scientific assessment. 7. The need for strict precaution in managing occupational exposure risks. • The emerging risk of carbon nanotubes, may only be the tip of the iceberg. We also find it bordering the ridiculous that we are only allowed one page, we have therefore send our full submission to the email address provided.

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Submission: 28

Organisation BASF SE

Type Business

publishing Yes

Comments BASF’s reply to DG Sanco’s Public Consultation on Nanotechnology For BASF chemical nanotechnology is an important field of activity.Parallel to the technological development we are participating in the safety research for nanomaterials, either by contributing to national or international research projects such as NanoCare or NanoSafe 2 or by own internal projects, like inhalaton toxicology of various nanoparticles, skin penetration, distribution in the body as well as mutagenicity and ecotoxicity of nanoparticles. Moreover we developed a short-term inhalation method to assess the toxicity of aerosols from nanomaterials. BASF has also expertise in occupational exposure measurement of nanoparticles.

We share our expertise with the international community in ISO TC 229 and the OECD WPMN. To be transparent towards the public, we publish the results of our safety research on our website www.basf.de/dialogue-nanotechnology/safety-research. We appreciate that SCENIHR refers in its opinion to our studies and we highly welcome its effort to provide the Commission with an updated scientific opinion on the risk assessment of products of nanotechnologies, since the knowledge has been growing very quickly. We value the opportunity to contribute with our expertise to the opinion. Generally we support the comprehensive and balanced analysis of the scienitific knowledge around nanomaterials. Early investigations on nanomaterial – toxicity often lack appropriate material and test-item characterization. Today we know that the characterization is essential. As a consequence many studies from the past are incomparable and even partly invalid. We recommend only to consider those studies in the scientific opinion, with a state-of-the art characterization and therefore comparable to other studies. In addition we support in principle the statement, that agglomerates or aggregates that have external dimensions well beyond 100 nm are not considered nanomaterials. SCENIHR proposes instead a specific surface area of > 60 m2/g . In our opinion, surface area and external dimension are not the only decisive criteria to determine the toxicity of nanomaterials Additonal health concerns may arrise from any additional functionalities of nanomaterials. Both biological as well as material properties of nanomaterials are governed by their functionalities (i.e. size, shape, surface, crystallinity, chemical composition). To address health concern appropriately the correlation between those different functionalities and change of biological effects should be one of the highest priorities of safety research, as a base of scientifically sound regulation. We support the proposal, to form “toxicological groups” for nanomaterials with considerably different properties such as carbon-nanotubes. Yet the number of groups is still very limited. At the moment a case by case consideration is the more appropriate approach, however we anticipate that with more knowledge, more grouping could be possible based on a scientific rational. We also support the SCENIHR opinion, that OECD guidelines in principle are appropriate for the risk assessment of nanomaterials. However identifying relevant addition health concerns of nanomaterials, in vitro methods should be further developed. Finally we agree that it is scientifically very interesting to understand all fates of nanomaterials in the environment. In the SCENIHR opinion many open questions are addressed. Nevertheless we emphasize that this research has to be prioritized by realistic exposure scenarios. Risk assessments are already feasable using currently available standard OECD guidelines with adaptations and without the extensive investigations of all possible effectes and fates in all environments. In order to realize nanotechnology and make use of its benefits, we should go for a pragmatic approach addressing specific health and environmental concerns based on specific material properties and exposure.

Submission: 29

Organisation People for the Ethical Treatment of Animals/Physicians Committee for Responsible Medicine

Type NGO

publishing Yes

Comments PETA and PCRM together represent more than 2 million members and supporters worldwide who are concerned about animal experiments conducted in the field of nanotechnology. We appreciate the opportunity to comment. I. Possible topics not previously covered A. Regular Review of Methods: PETA recommends that documents and recommendations related to standards for nanomaterials (NM) be updated regularly so that they remain current and nanospecific. B. Standardization of Nanomaterial Characterization: EC must recommend standard methods for NM characterization, detection, and environmental/workplace monitoring, and should also devise an ordered protocol for efficient application of these methods in order to reduce experimental redundancy and down-stream animal use. II. Main potential risks from the use of nanomaterials A. Endotoxin Detection: NM preparations often exhibit endotoxin activity that can confound results of other toxicity assessments. Therefore, it is recommended that NM be tested for endotoxin activity prior to any other toxicological testing. In order to avoid the use of rabbits for endotoxin detection, the Limulus Amebocyte Lysate (LAL) or in vitro tests for pyrogen/endotoxin detection using human whole blood should be employed. An

international standard for NM using the LAL method rather than the rabbit is currently underway (ISO/DIS 29701) . B. Other Toxicity Traditional animal-based test methods are inappropriate for NM for several reasons. Dosing, delivery, and tracking of nanoparticles are not reliably measureable in vivo , and the resulting animal data has proven to be inaccurate , open to interpretation, and not reliably reproducible. In vivo methods have not been validated for NM and there is little reason to invest in these methods for the new field of nanotechnology. Instead, preference should be given to recently-developed technology that is more promising with regard to providing accurate toxicological data for NM. 1. Systemic Toxicity Via Differing Routes of Exposure: a. Pulmonary: Unique properties of NM create challenges for in vivo dose and delivery including the degree of aggregation/agglomeration, particle shape, dose rate, and directed delivery to specific pulmonary regions. Each of these factors coupled with the lung's response to receiving a highly concentrated liquid bolus (which by default results in an inflammatory reaction) greatly affects the perceived toxicity in vivo. There is a concerted effort to begin using human cell-based co-cultures to assay potential toxicity for this exposure route , . , b. Dermal: In vitro human skin-based methods have already been put to use for NM . For all assessments of dermal toxicity, a tiered approach should be implemented that first assesses dermal absorption in vitro (e.g. OECD TG 428 which uses human skin samples as a component of the skin absorption testing strategy). 2. Neurotoxicity: Cell co-cultures that model the blood-brain barrier and are capable of predicting nanoparticle transcytosis and toxicity have been developed by Lu et al . Comparison between the in vitro results and results from in vivo tests in rats show data concordance. 3. Developmental Toxicity: Ex vivo human placental perfusion models have proven useful in determining whether small molecules and nanoparticles are able to cross the placental barrier , . III. Issues to be discussed at the hearing Tiered Screening and Testing for Nanomaterials: Hazard data should be developed through a step-wise process, beginning with a general assessment of cytotoxic potential using in vitro and in silico methods. Once satisfied that the general potential for toxicity of a given nanomaterial is sufficiently low to be further developed, additional in vitro assays with greater specificity should then be applied to assess mechanisms of action and the effects on specific toxicity pathways. Sincerely, Samantha Dozier, Ph.D., PETA Chad Sandusky, Ph.D., PCRM

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Submission: 30

Organisation Technological Centre LEITAT

Type Private Organisation

publishing Yes

Comments In the technological centre LEITAT (Barcelona), we are interested in the global evaluation of the potential human health and environmental impacts of nanomaterials derived from their use, recycling and final treatment (covering the whole life cycle of these novel materials). The great potential of nanomaterials has been transferred to almost all the industrial sectors to generate innovative products or to improve the existing ones. Since one of the activities of LEITAT is to transfer technology based on nanomaterials to industries, the nanotechnology group is interested in the control of the toxicity of these novel materials included in industry processes and products in order to inform about their risks. The control over the nanotoxicity of these materials will include exhaustive evaluations of the different nanomaterials during their whole life cycle for the developing of more sustainable products. From our experience, we would like to point out the need of: - Knowledge about the evolution of the toxicity of nanomaterials during their transformations when included into matrices (nanocomposites), and during the aging processes. - Technological solutions for recycling and final treatment (inertization) of nanomaterials that present advantages respect to the existing ones.

Submission: 31

Organisation People for the Ethical Treatment of Animals/Physicians Committee for Responsible Medicine

Type NGO

publishing Yes

Comments PETA and PCRM together represent more than 2 million members and supporters worldwide who are concerned about animal experiments conducted in the field of nanotechnology. We appreciate the opportunity to comment. I. Possible topics not previously covered A. Regular Review of Methods: PETA recommends that documents and recommendations related to standards for nanomaterials (NM) be updated regularly so that they remain current and nanospecific. B. Standardization of Nanomaterial Characterization: EC must recommend standard methods for NM characterization, detection, and environmental/workplace monitoring, and should also devise an ordered protocol for efficient application of these methods in order to reduce experimental redundancy and down-stream animal use. II. Main potential risks from the use of nanomaterials A. Endotoxin Detection: NM preparations often exhibit endotoxin activity that can confound results of other toxicity assessments. Therefore, it is recommended that NM be tested for endotoxin activity prior to any other toxicological testing. In order to avoid the use of rabbits for endotoxin detection, the Limulus Amebocyte Lysate (LAL) or in vitro tests for pyrogen/endotoxin detection using human whole blood should be employed. An international standard for NM using the LAL method rather than the rabbit is currently underway (ISO/DIS 29701) . B. Other Toxicity Traditional animal-based test methods are inappropriate for NM for several reasons. Dosing, delivery and tracking of nanoparticles are not reliably measureable in vivo , and the resulting animal data has proven to be inaccurate , open to interpretation, and not reliably reproducible, In vivo methods have not been validated for NM and there is little reason to invest in these methods for the new field of nanotechnology. Instead, preference should be given to recently-developed technology that is more promising with regard to providing accurate toxicological data for NM. 1. Systemic Toxicity Via

Differing Routes of Exposure: a. Pulmonary: Unique properties of NM create challenges for in vivo dose and delivery including the degree of aggregation/agglomeration, particle shape, dose rate, and directed delivery to specific pulmonary regions. Each of these factors coupled with the lung's response to receiving a highly concentrated liquid bolus (which by default results in an inflammatory reaction) greatly affects the perceived toxicity in vivo. There is a concerted effort to begin using human cell-based co-cultures to assay potential toxicity for this exposure route , . , b. Dermal: In vitro human skin-based methods have already been put to use for NM . For all assessments of dermal toxicity, a tiered approach should be implemented that first assesses dermal absorption in vitro (e.g. OECD TG 428 which uses human skin samples as a component of the skin absorption testing strategy). 2. Neurotoxicity: Cell co-cultures that model the blood-brain barrier and are capable of predicting nanoparticle transcytosis and toxicity have been developed by Lu et al . Comparison between the in vitro results and results from in vivo tests in rats show data concordance. 3. Developmental Toxicity: Ex vivo human placental perfusion models have proven useful in determining whether small molecules and nanoparticles are able to cross the placental barrier , . III. Issues to be discussed at the hearing Tiered Screening and Testing for Nanomaterials: Hazard data should be developed through a step-wise process, beginning with a general assessment of cytotoxic potential using in vitro and in silico methods. Once satisfied that the general potential for toxicity of a given nanomaterial is sufficiently low to be further developed, additional in vitro assays with greater specificity should then be applied to assess mechanisms of action and the effects on specific toxicity pathways. Sincerely, Samantha Dozier, Ph.D., PETA Chad Sandusky, Ph.D., PCRM

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http://www.iso.org/iso/iso_catalogue/catalogue_ics/catalogue_detail_ics.htm?ics1=7&ics2=30&ics3=&csnumber=45640 Borm, P. et al. The potential risks of nanomaterials: a review carried out for ECETOC. Part Fibre Toxicol. 2006; 3: 11 Oberdorster, G. et al. Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles. Environ Health Perspect. 2005 July; 113(7): 823–839. Maynard, A. et al. Safe Handling of Nanotechnology. Nature. 2006 444 (16): 267-9. Trop, M., et al., Silver coated dressing caused raised liver enzymes and argyria-like symptoms in burn patient. Journal of Trauma-Injury Infection and Critical Care, March 2006. Maynard, A. et al. Safe Handling of Nanotechnology. Nature. 2006 444 (16): 267- Lam, C.-W., James, J. T., McCluskey, R., and Hunter, R. L. (2004). Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation. Toxicol. Sci. 77, 126–134. Tsuji, et al. Research Strategies for Safety Evaluation of Nanomaterials, Part IV: Risk Assessment of Nanoparticles. ToxSci 2006, 89(1):42-50. Geys J, Nemery B, Hoet PH. Optimisation of culture conditions to develop an in vitro pulmonary permeability model. Toxicol In Vitro. 2007; 21(7): 1215-9. Bur M, Rothen-Rutishauser B, Huwer H, Lehr CM. A novel cell compatible impingement system to study in vitro drug absorption from dry powder aerosol formulations. Eur J Pharm Biopharm. 2008 Aug 17. Alfaro-Moreno, E. et al. Co-cultures of multiple cell types mimic pulmonary cell communication in response to urban PM10. Eur Respir J. 2008; 32:1184-1194. Rothen-Rutishauser B et al. A newly developed in vitro model of the human epithelial airway barrier to study the toxic potential of nanoparticles. ALTEX. 2008;25(3):191-6. Mavon A, Miquel C, Lejeune O, Payre B, Moretto P. In vitro percutaneous absorption and in vivo stratum corneum distribution of an organic and mineral sunscreen. Skin Pharmacol. Physiol. 2007; 20: 10-20. Baroli B, Ennas M, Loffredo F et al. Penetration of metallic nanoparticles inhuman Full thickness skin. Soc. Investig. Dermato. 2007; 127: 1701-1712. Wissing S, Mueller R. Solid lipid nanoparticles as carrier for sunscreens: in vitro release and in vivo skin penetration. J. Contr. Release. 2002; 81: 225-233 Lu W, Tan YZ, Jiang XG. Establishment of coculture model of blood-brain barrier in vitro for nanoparticle's transcytosis and toxicity evaluation. Yao Xue Xue Bao. 2006 Apr;41(4):296-304. Myllynena, P, et al. Kinetics of gold nanoparticles in the human placenta. Reproductive ToxicologyVolume 26, Issue 2, October 2008, Pages 130-137 Hnat M, Bawdon RE. Transfer of meropenem in the ex vivo human placenta perfusion model. Infect Dis Obstet Gynecol. 2005 Dec;13(4):223-7.

Submission: 32

Organisation Eucomed

Type Business

publishing Yes

Comments Eucomed wishes to support the comments introduced by the Nanotechnology Industries Association (NIA) Eucomed represents 4500 designers, manufacturers and suppliers of medical technology used in the diagnosis, prevention, treatment and amelioration of disease and disability. Eucomed members include national trade and pan-European product associations and internationally active manufacturers of all types of medical technology. The mission of Eucomed is to improve patient and clinician access to modern, innovative and reliable medical technology.

Submission: 33

name Dr. Rolf F. Hertel

Individual

publishing Yes

Comments There are manifold ideas of possible applications of nanomaterials/nanoscalic instruments which would be desirable or could be in use in future. A survey could be useful to find out whether these ideas have a realistic chance to be realized.

Submission: 34

Organisation European Tyre & Rubber Manufacturers' Association

Type Business

publishing Yes

Comments DEFINITIONS/ DISTINTIONS BETWEEN NANO-OBJECTS (NANO-PARTICLES) AND NANO-STRUCTURED MATERIALS In order to properly identify and assess the risks associated to specific nanotechnologies, It is of high importance to adopt complete and precise definitions . A clear distinction should be made between: - a. Nano-objects (in some case associated to the term nanoparticles), defined as “material with one, two or three external dimensions at the nanoscale” (ISO), i.e. as materials constituted by isolated objects with very small dimensions. - b. Nano-structured materials, defined as materials “having an internal or surface structure at the nanoscale” (OECD), e.g. exhibiting cavities of small dimensions. Distinguishing (at least) between these two groups of “nanomaterials” is very important, as the “knowledge gap” in risk assessment methodologies identified by the Scientific Committee of the Commission essentially applies to nano-objects. In particular: - “The majority of concerns about the health and environmental risks of nanomaterials, and indeed the majority of data and information on this subject, relate to nanoparticles. It is recognised, of course, that these [nanoparticles] are not necessarily the only forms of nanomaterials and that solid materials with surface nanoscale features [...] may also have specific and unique physicochemical properties. However, in order to avoid confusion in an area where there is so little data, and to maintain relevance to the questions concerning

the Technical Guidance Documents, this Opinion refers only to nanoparticles". [SCENIHR - Scientific Committee on Emerging and Newly-Identified Health Risks, The appropriateness of the risk assessment methodology in accordance with the Technical Guidance Documents for new and existing substances for assessing the risks of nanomaterials, 21-22 June 2007]. - "The health and environmental hazards were demonstrated for a variety of manufactured nanomaterials. The identified hazards indicate potential toxic effects of nanomaterials for man and environment. However, it should be noted that not all nanomaterials induce toxic effects. Arguably, some manufactured nanomaterials have been in use for a long time (carbon black, TiO2) and show low toxicity" [SCENIHR - Scientific Committee on Emerging and Newly Identified Health Risks, Risk assessment of products of nanotechnologies, 19 January 2009]. Specific activities on this area are also conducted within ISO TC 229.

Submission: 35

Name Bernd Rainer Mueller

Individual

publishing Yes

Comments Normung ist nur ein Teil der Regulierungsmöglichkeiten für eine Technologie. Bei der Festlegung auf Nachhaltigkeit müssen zu Regulierungen folgende strategischen Überlegungen sichtbar werden. Verhalten sich Nanopartikel auch unter extremen Umweltbedingungen weitgehend stabil bzw. treten bei dem Eintritt in die Umwelt sehr schnelle Reaktionsprozesse auf, die anschließend stabil bleiben, sind geringe Umweltfolgen zu erwarten, weil die bisher bekannten Eigenschaften der Nanopartikel (hohe Reaktionsfähigkeit und geringe Größe, die zur Überwindung bekannter biologischer Schranken führen können), nicht mehr gegeben sind. Durch Parameter zur Toxizität und der dadurch entstehende Risiken lässt sich ein angestrebtes Schutzniveau beschreiben. Entscheidende Parameter für eine Umweltrelevanz können sein: - physikalisch-chemisch (z. B. Energiezufuhr kann Moleküle/Nanopartikel anregen, andere Strukturen aufzubauen, Reaktionsfähigkeit, Löslichkeit, Struktur) - biologisch (z. B. Membrangängigkeit, Diffusionseigenschaften, biologische Aktivität) Die bisherigen Verfahren zum Nachweis und zur Messung allgemein bzw. speziell von Nanopartikeln gehen vom Prinzip „Sammeln-Zählen-Charakterisieren" aus und beschreiben damit in erster Linie die Auswirkungen von punktbezogenen bzw. flächenbezogenen Quellen in einem Zeitraum. Bezüglich des Zusammenhangs „Nanopartikel mit aktiven biologischen Bausteinen" sind neben Größe-, Anzahl-, Charakterisierungs-Parametern zusätzliche Prozess-Parameter zu entwickeln, die sich auf wirkungs- und dosisbezogene Eigenschaften in biologischen Systemen beziehen. Dabei stellen sich grundsätzlichen Fragen, um wesentliche Schlüsselinformationen zu erhalten: Welche kritischen Endpunkte unter Gesundheitsaspekten weisen einen hohen Stellenwert auf (reaktionsbezogene, zerstörende (toxische)? Welche Zielstrukturen im Gesundheitsschutz z. B. Haut, Gehirn, Lunge, sollen bei der Exposition mit Nanopartikeln einen hohen Stellenwert aufweisen? Welche Zielstrukturen im Umweltschutz z. B. Aerosole, Luftqualität sollen bei der Exposition mit Nanopartikeln einen hohen Stellenwert aufweisen? Welche Daten im Zusammenhang mit Nanopartikel können für den Umwelt- und Gesundheitsschutz eine große Bedeutung erhalten? Wie können diese Daten gewonnen werden, um daraus Information und gesichertes Wissen z. B. eine Nano-Datenbank zu erhalten? Welche Eigenschaften der Nanopartikel sollen bezüglich des Umwelt-/Gesundheitsschutzes einen hohen Stellenwert aufweisen? Wie soll ein geringes/hohes Gefährdungspotential dieser Eigenschaften nachgewiesen werden? Welche Parameter dieser Eigenschaften von Nanopartikeln im Bereich „Sammeln-Zählen-Charakterisieren" und „Prozesse" sind zur Einschätzung des Gefährdungspotentials geeignet? Welche Parameter können davon in Nanostrukturen tatsächlich gemessen werden? Welche Messverfahren stehen zur Verfügung d. h. was wird bei instabilen Vorgängen tatsächlich gemessen? (z. B. Parameter bezüglich eines aktuellen Prozessstandes oder eines weitgehend abgeschlossenen Prozesses) Welche Proben (Präparation, Entnahme, Vorbereitung, Zeiten, Messverfahren) können bei instabilen Vorgängen geeignet sein, um aussagekräftige Messergebnisse zu erhalten? Welche Parameter sollten grundsätzlich erfasst und in Datenbanken öffentlich zugänglich sein, um bei später auftretenden negativen Entwicklungen einen Zusammenhang mit Grundstoffen bzw. Produkten zu erkennen?

Submission: 36

Organisation German Chemical Industry Association (VCI)

Type Business

publishing Yes

Comments Possible topics for the Scientific Committees and potential risks of nanotechnology VCI has identified six relevant areas of interest for further clarification by the Scientific Committees: 1. Refinement of analytical methods to differentiate between human exposure to natural and man-made nanoparticles 2. To further clarify the association and mechanistic link of the presence of nanoparticles in airborne dusts and the incidence of cardio-vascular disease [1] 3. To improve the mechanistic understanding of nanoparticles' potential to alter human DNA 4. To gain a better understanding of the toxicokinetics of nanoparticles, i.e. their translocation in biological systems 5. Refinement of the understanding of if and how nanoparticles' behaviour could be altered in the environment 6. Improvement of the understanding of nanomaterials and particles behaviour in in-vitro system to refine the existing test methods to evaluate their applicability [2]. Specific Comments on the SCENIHR Report, published February 2009 • potential risks as described in the report could only occur with specific "nano-objects" including their aggregates/agglomerates and should not be generalised to include all nanomaterials. • systematic generalisation of the potential hazardous effects of nanomaterials is problematic because it is not possible to conclude that if a specific nanomaterial exhibits effects for certain endpoints, than all nanomaterials have the potential to display the same effects. Chemical Industry agrees that risk assessment (RA) can only be done of case-by-case basis. • the Expert Judgement Matrix, as proposed by SCENIHR, may therefore only be used to evaluate a possible way forward to conduct a RA. In the same way, risk management measures for nanomaterials cannot be categorised and can only be derived case-by-case. • cardiovascular effects of nanomaterials are emphasised even though the scientific basis for such an opinion is limited. Such scientific questions are generally not specific for man-made nanomaterials but a general issue concerning small ambient particles esp. in smoky atmospheres instead. • is highlighting the need for finding agreement on reference materials in the field of nanomaterials and manufactured nanoparticles while recognising that the progress is hampered by the absence of well defined parameters to measure and of standardised test protocols. The OECD has agreed upon 14 "representative nanomaterials" meant to fill these knowledge gaps and create an information basis to further refine scientific knowledge on these materials. OECD and ISO have not come any closer in defining nanospecific properties. • detection and assessment of manufactured nanoparticles in the environment principally rely on the same analytical procedures and assessment strategies as currently applied for exposition assessment of nanoparticles at workplace atmospheres. E.g. the intake of natural nanoparticles in aqueous media is well understood and documented [3]. Research needs can be identified referring to release of particles in the end-of-life-phase of composite materials and for determination of the natural background burden. • states that one of the main limitations is the lack of exposure and dosimetry data both for humans and the environment. OECD has concluded in a workshop [4] that measurement techniques and devices are in principle available and have been tested for measurement of nanoparticles. In specific cases, test methods have to be adapted for test sampling and sample preparation prior to material characterisation for toxicological and eco-toxicological testing. The Chemical Industry commits itself to additional physicochemical testing to better characterise the substances at nanoscale to the extent needed for the RA and for compiling in the Safety Data Sheet (SDS) in accordance with findings of ongoing OECD investigations.

References References 1. "The potential risks of nanomaterials: a review carried out for ECETOC" Paul JA Borm, David Robbins, Stephan Haubold, Thomas Kuhlbusch, Heinz Fissan, Ken Donaldson, Roel Schins, Vicki Stone, Wolfgang Kreyling, Jurgen Lademann, Jean Krutmann, David Warheit and Eva Oberdorster, Particle and Fibre Toxicology 2006, 3:11 doi:10.1186/1743-8977-3-11; Paul J. Borm: "Future interactions in Particle Toxicology: the role of PFT", Particle and Fibre Toxicology 2008, 5:5 doi:10.1186/1743-8977-5-5; Mossman: "Mechanisms of action of inhaled fibers, particles and nanoparticles in lung and cardiovascular diseases", Particle and Fibre Toxicology 2007, 4:4

doi:10.1186/1743-8977-4-4 2. Publications by Iseult Lynch and Kenneth Dawson (NanoInteract project) 3. International Water Association – IWA Report 4. Additionally in the OECD workshop on exposure measurement and exposure mitigation from October 2008 it has been concluded that “Measurement techniques and devices are available in principle and have been tested to measure nanoparticles. But standard measurement processes have to be agreed on that are founded on a reliable basis on reference materials and measurement calibration.” [OECD Working Party on Manufactured Nanomaterials (WPMN) Workshop on “Exposure Assessment and Exposure Mitigation” 20 October 2008, Frankfurt, Germany, Notes] Statement on Test Guidelines VCI would like to stress that subgroup of the OECD WPMN (SG4) concluded that the OECD guidelines are appropriate for investigating the health effects of nanomaterials. This is confirmed by SCENIHR: "Many of the currently available OECD guidelines for the testing of chemicals are likely to be adequate to detect potential hazards of manufactured nanomaterials as well (page 23).” As the relevance of interactions with protein studied by in vitro methods for in vivo toxicity testing cannot be justified according to current knowledge, further scientific research may be recommended. Definition To further develop and harmonise instruments for nanomaterials testing, the chemical industry is deeply engaged in the standardisation process at international (ISO), European (CEN), and at national level. SCENIHR proposes an extension of the definition for nanomaterials that is not based on size alone but also including the following criteria: - substances smaller than about 100 nm and their aggregates and agglomerates and - Specific surface area (by BET) larger than 60 m2/g. While this additional surface area criterion may be meaningful for those adverse effects where there is appropriate scientific evidence that the mechanism of toxicity is mediated by surface activity, an increase in surface area does not necessarily correlate with increased hazardous properties. Therefore VCI’s is not convinced that specific surface area should be a general criterion included in the definition. Not every nanomaterial described in literature is a commercial product. The majority of existing man-made nanomaterials are not commercialised in the form that they appear in the scientific reports. To ensure safe use, the risk assessment has to consider the form and conditions in which the nanomaterial is used. Furthermore, VCI shares the SCENIHR opinion that nanomaterials are similar to “normal” substances as some nanomaterials may be (eco)toxic, and some may not. As SCENIHR states that “… The significance of nanomaterial coating for ... risk assessment is clear, as it implies that detailed characterisation of the nanoparticles in the relevant biological environment is necessary ...” (page 53) the release of nanoparticulate matter from paint and coatings has to be considered in risk assessment. This issue has been taken up by the study of the German Industry Association of Paint and Lacquers (Lackverband) that has been recently published and has quantified nanoparticle release into air from surface coatings revealing that there is no significant abrasion under conditions of product. According to the findings the mass of purposely abraded particles depends on substrate and coating but there is no significant correlation to nanoparticle content.

Submission: 37

Organisation France Nature Environnement Federation

Type NGO

publishing Yes

Comments Failure of identifying risk exposure in the occupational and safety health context Due to the potential risk exposure described in the SCENIHR report, the France Nature Environnement Federation asks for urgent measures to protect workers. 1. The SCENIHR report fails to identify the risks of manipulating unlabelled nanomaterials and nanoparticules. As a prevention approach based on risk assessment is the cornerstone of the European approach to OSH, all workers in contact with nanoparticles and nanomaterials must benefit from: ? Information and training on good practices, including exploding risks of specific nanomaterials; ? A clear and visible label which is an essential measure for tracing the products at each stage of the life cycle, including production, transformation, storage…. OSH services, Labour Inspectorates, Social Partners must be trained urgently on the specific risks of nanomaterials and specific exposure evaluation. OSHA, the European Agency for Safety and Health at Work, could play a leading role in following cohorts of exposed workers at the European level. 2. The

SCENIHR report fails to identify the risks in case of emergency : ? Civil protection workers must be especially trained and equipped to provide assistance in contaminated conditions; ? An updated list of workplaces using nanomaterials must be available for the emergency centres to alert the intervention teams; ? Hospitals must have specific treatments for victims highly contaminated by nanoparticles.

References European Agency for Safety and Health at Work http://osha.europa.eu/en/riskobservatory/teaser/nanotechnologies European civil protection http://ec.europa.eu/environment/civil/index.htm

Submission: 38

Organisation Cefic

Type NGO

publishing Yes

Comments Cefic has identified five relevant areas of interest for further clarification: 1. Refinement of analytical methods to differentiate between human exposure to natural and man-made nanoparticles 2. To further clarify the association and mechanistic link of the presence of nanoparticles in airborne dusts and the incidence of cardio-vascular disease [1] 3. To improve the mechanistic understanding of nanoparticles' potential to alter human DNA 4. To gain a better understanding of the toxicokinetics of nanoparticles, i.e. their translocation in biological systems 5. Refinement of the understanding of if and how nanoparticles' behaviour could be altered in the environment 6. Improvement of the understanding of nanomaterials and particles behaviour in in-vitro system to refine the existing test methods to evaluate their applicability [2] Specific Comments on the SCENIHR Report, published February 2009 • potential risks as described in the report could only occur with specific "nano-objects" including their aggregates and agglomerates based on their small size and should not be generalised to include all nanomaterials. • systematic generalisation of the potential hazardous effects of nanomaterials is problematic because it is not possible to conclude that if a specific nanomaterial exhibits effects for certain endpoints, than all nanomaterials have the potential to display the same effects. The Chemical Industry agrees that a risk assessment can only be done of case-by-case basis. • the Expert Judgement Matrix, as proposed by SCENIHR, may therefore only be used to evaluate a possible way forward to conduct a risk assessment. In the same way, risk management measures for nanomaterials cannot be categorised and can only be derived from a thorough case-by-case assessment. • the commonly believed cardiovascular effects of nanomaterials are emphasised even though the scientific basis for such an opinion is limited. Such scientific questions are generally not specific for man-made nanomaterials but a general issue concerning small ambient particles esp. in smoky atmospheres instead. • is highlighting the need for finding agreement on reference materials in the field of nanomaterials and manufactured nanoparticles while recognising that the progress is hampered by the absence of well defined parameters to measure and of standardised test protocols. The OECD has agreed upon 14 "representative nanomaterials" meant to fill these knowledge gaps and create an information basis to further refine scientific knowledge on these materials. OECD and ISO have not come any closer in defining nanospecific properties. • detection and assessment of manufactured nanoparticles in the environment principally rely on the same analytical procedures and assessment strategies as currently applied for exposition assessment of nanoparticles at workplace atmospheres. E.g. the intake of natural nanoparticles in aqueous media is well understood and documented [3]. Research needs can be identified referring to release of particles in the end-of-life-phase of composite materials and for determination of the natural background burden. • states that one of the main limitations is the lack of exposure and dosimetry data both for humans and the environment. OECD has concluded in a workshop [4] that measurement techniques and devices are in principle available and have been tested for measurement of nanoparticles. In specific cases, test methods have to be adapted for test sampling and sample preparation prior to the characterisation of the material for toxicological and eco-toxicological testing. The Chemical Industry commits itself to additional physicochemical testing to better characterise the substances at nanoscale to the extent needed for the risk assessment and for compiling in the Safety Data Sheet (SDS) in accordance with the findings of the ongoing OECD

investigations.

References References 1. “The potential risks of nanomaterials: a review carried out for ECETOC” Paul JA Borm, David Robbins, Stephan Haubold, Thomas Kuhlbusch, Heinz Fissan, Ken Donaldson, Roel Schins, Vicki Stone, Wolfgang Kreyling, Jurgen Lademann, Jean Krutmann, David Warheit and Eva Oberdorster, Particle and Fibre Toxicology 2006, 3:11 doi:10.1186/1743-8977-3-11; Paul J. Borm: “Future interactions in Particle Toxicology: the role of PFT”, Particle and Fibre Toxicology 2008, 5:5 doi:10.1186/1743-8977-5-5; Mossman: “Mechanisms of action of inhaled fibers, particles and nanoparticles in lung and cardiovascular diseases”, Particle and Fibre Toxicology 2007, 4:4 doi:10.1186/1743-8977-4-4 2. Publications by Iseult Lynch and Kenneth Dawson (NanoInteract project) 3. International Water Association – IWA Report 4. Additionally in the OECD workshop on exposure measurement and exposure mitigation from October 2008 it has been concluded that “Measurement techniques and devices are available in principle and have been tested to measure nanoparticles. But standard measurement processes have to be agreed on that are founded on a reliable basis on reference materials and measurement calibration.” [OECD Working Party on Manufactured Nanomaterials (WPMN) Workshop on “Exposure Assessment and Exposure Mitigation” 20 October 2008, Frankfurt, Germany, Notes] Statement on Test Guidelines Cefic would like to stress that subgroup of the OECD WPMN (SG4) concluded that the OECD guidelines are appropriate for investigating the health effects of nanomaterials. This is confirmed by SCENIHR: "Many of the currently available OECD guidelines for the testing of chemicals are likely to be adequate to detect potential hazards of manufactured nanomaterials as well (page 23).” Definition To further develop and harmonise instruments for nanomaterials testing, the chemical industry is deeply engaged in the standardisation process at international (ISO), European (CEN), and at national level. SCENIHR proposes an extension of the definition for nanomaterials that is not based on size alone but also including the following criteria: - substances smaller than about 100 nm and their aggregates and agglomerates and - Specific surface area (by BET) larger than 60 m2/g. While this additional surface area criterion may be meaningful for those adverse effects where there is appropriate scientific evidence that the mechanism of toxicity is mediated by surface activity, an increase in surface area does not necessarily correlate with increased hazardous properties. Therefore Cefic’s is not convinced that specific surface area should be a general criterion included in the definition. Not every nanomaterial described in literature is a commercial product. The majority of existing man-made nanomaterials are not commercialised in the form that they appear in the scientific reports. To ensure safe use, the risk assessment has to consider the form and conditions in which the nanomaterial is used. Furthermore, Cefic shares the SCENIHR opinion that nanomaterials are similar to “normal” substances as some nanomaterials may be (eco)toxic, and some may not. As SCENIHR states that “… The significance of nanomaterial coating for ... risk assessment is clear, as it implies that detailed characterisation of the nanoparticles in the relevant biological environment is necessary ...” (page 53) the release of nanoparticulate matter from paint and coatings has to be considered in risk assessment. This issue has been taken up by the study of the German Industry Association of Paint and Lacquers (Lackverband) that has been recently published and has quantified nanoparticle release into air from surface coatings revealing that there is no significant abrasion under conditions of product. According to the findings the mass of purposely abraded particles depends on substrate and coating but there is no significant correlation to nanoparticle content.

Submission: 39

Organisation Bayerisches Staatsministerium für Umwelt und Gesundheit

Type Public authority

publishing Yes

Comments Das Bayerische Staatsministerium für Umwelt und Gesundheit hat zwei Themenfelder identifiziert, die in den bisherigen Gutachten von SCENIHR, SCCS und EFSA noch nicht ausreichend behandelt wurden und bei der Anhörung diskutiert werden sollten: 1. Nanomaterialien in verbrauchernahen Produkten Synthetische Nanomaterialien in Verbraucherprodukten (z. B. in

Reinigungs- und Imprägniersprays, die potentiell bei der Verwendung freigesetzt werden können), wurden bisher nicht berücksichtigt. Produkte sind auf dem Markt mit dem Zusatz „Nano“ gekennzeichnet, wobei nicht klar ist, ob Nanopartikel (NP) darin enthalten sind, oder dies nur zu Werbezwecken geschieht. Ggf. sind auch nanoskalige Materialien in Produkten ohne Hinweis enthalten. Unklar ist, ob aus diesen Sprays bei richtigem oder unsachgemäßem Umgang unlösliche oder biologisch beständige Nanomaterialien freigesetzt werden, die vom Verbraucher inhalativ aufgenommen werden können. Da nicht bekannt ist, ob und welche Nanopartikel enthalten sind, sind mögliche gesundheitliche Auswirkungen nicht abschätzbar. Solche Verbraucherprodukte sollten von staatlichen Kontrollbehörden untersucht werden, um das Ausmaß des Einsatzes von Nanomaterialien zu erfassen. Entsprechende Methoden sind zu entwickeln. Das Bayerische Landesamt für Gesundheit und Lebensmittelsicherheit untersucht derzeit in Kooperation mit der Ludwig-Maximilians-Universität München in zwei Projekten Exposition und mögliche gesundheitliche Risiken gegenüber verbrauchernahen Produkten. Es sollte zudem eine Kennzeichnung verbrauchernaher Produkte ähnlich der Neufassung der EU-Kosmetikverordnung diskutiert werden, wenn unlösliche oder biologisch beständige, absichtlich hergestellte Nanomaterialien enthalten und vom Verbraucher aufgenommen werden könnten. Die Unbedenklichkeit neuartiger Materialien muss geprüft sein, bevor diese in Verbraucherprodukten auf den Markt kommen. 2. Nanomaterialien in Lebens- und Nahrungsergänzungsmitteln Es ist derzeit davon auszugehen, dass sich zahlreiche Nahrungsergänzungsmittel und Verpackungsmaterialien im Kontakt mit Lebensmitteln auf dem Markt befinden, die mit „Nano“ beworben werden, wobei auch hier nicht klar ist, ob NP darin enthalten sind, oder dies nur zu Werbezwecken geschieht. Es ist auch nicht ausgeschlossen, dass sich Lebens- und Futtermittel ohne Deklaration im Handel befinden, obwohl sie NP enthalten, und der Verbraucher unwissentlich exponiert wird. Staatliche Kontrollbehörden sollten deshalb auf dem Markt befindliche Lebens- und Futtermittel auf das Vorhandensein von NP untersuchen. Unseres Erachtens ist die Untersuchung von z.B. Nahrungsergänzungsmitteln, Lebensmitteln in Kontakt mit innovativen Verpackungsmaterialien und Lebensmittelzusatzstoffen; z.B. für Lebens- oder Futtermittel mit besonders guten Fließeigenschaften von großem Interesse. Um der staatlichen Lebensmittelüberwachung eine Abschätzung der Exposition der Verbraucher mit Nanopartikeln über Lebensmittel zu ermöglichen, ist es nötig, geeignete Untersuchungsmethoden zum quantitativen Nachweis von in Lebens- und Futtermitteln enthaltenen Nanomaterialien verfügbar zu machen. Die Sachgebiete Umweltmedizin und Nahrungsergänzungsmittel/ Novel Food des Bayerischen Landesamts für Gesundheit und Lebensmittelsicherheit werden in einem neuen Projekt „Lebensmittelsicherheit und Nanotechnologie (LENA)“ in Zusammenarbeit mit dem Fraunhofer Institut für Verfahrenstechnik und Verpackung (IVV) die Migration von Nanomaterialien aus Verpackungen untersuchen und Nahrungsergänzungsmittel auf NP überprüfen. Als Vorsorgemaßnahme sollte diskutiert werden, dass vor dem Einsatz absichtlich hergestellter, unlöslicher oder biologisch beständiger nanoskaliger Materialien in Lebensmitteln deren Unbedenklichkeit unabhängig von der Muttersubstanz toxikologisch überprüft wird und dies ggf. auch gesetzlich sicher gestellt wird. Außerdem sollte über eine entsprechende Deklarierung solcher synthetischer NP in Lebensmitteln diskutiert werden.

Submission: 40

Organisation ASTM International

Type NGO

publishing Yes

Comments ASTM International welcomes the opportunity to respond to the European Commission’s public consultation that will serve as a basis for the Scientific Hearing on Nanotechnology. ASTM International is a nonprofit organization with more than 30,000 volunteer technical experts from around the world who develop international standards for over 100 industries. As a leading developer of nanotechnology standards, we help researchers, regulatory authorities, and other stakeholders worldwide by supplying important safety standards, material specifications, guides and test methods. Over 195 technical experts participate on ASTM Committee E56 on Nanotechnology, representing regulatory bodies, industry groups and academic institutions from around the globe, including European Union

Member States. We welcome SCENIHR's groundbreaking research on nanotechnology and echo its opinion of January 2009, that there must be a greater push in developing standardized methods and definitions in this area. ASTM International's Committee E56 has been dedicated to researching exactly these issues since 2005. In 2006, ASTM published standard E 2456, Terminology for Nanotechnology. This standard (available to the public at no charge) is a globally recognized nanotechnology terminology document developed in partnership with the Institute of Electrical and Electronics Engineers, the American Society of Mechanical Engineers, NSF International, Japan's National Institute of Advanced Industrial Science and Technology, Semiconductor Equipment and Materials International, and the American Institute of Chemical Engineering. More recently, ASTM Committee E56 continues to addresses issues related to standards and guidance materials for nanotechnology and nanomaterials and has published international methods for nanoparticle biocompatibility testing, the use of which could pave the way for commercially available nanoscale cancer drugs. Additionally, the Committee published E2535, Standard Guide for Handling Unbound Engineered Nanoscale particles in Occupational Settings, which describes actions that a user could take to minimize exposure to unbound, engineered nanoscale particles in various occupational settings. ASTM International believes that European policymakers, researchers and manufacturers should have the flexibility to utilize any international standard that meets health and safety needs, not just those that meet the requirements of relevant Commission directives. In a fast moving and largely unexplored area such as nanotechnology, it is particularly important that decisions regarding the use of standards be made based on important science-based factors such as technical quality and relevance. We propose that the Commission empower the institutions to reference relevant international standards developed by bodies that satisfy the principles and procedures for the elaboration of international standards established by the WTO Committee on Technical Barriers to Trade. The Commission already relies on such international standards in other areas, such as the automobile and petroleum sectors, to help meet regulatory needs and similar arrangements are common in other jurisdictions. This regulatory flexibility would not impede the functioning of the common market nor threaten public safety, quite the opposite. The ability to reference relevant international nanotechnology standards would better equip the Commission and the European Union to respond to new challenges and opportunities created by advanced technologies of tomorrow.

Submission: 41

Organisation Fédération France Nature Environnement

Type NGO

publishing Yes

Comments Le SCENIHR n'identifie pas les types d'acteurs en mesure d'évaluer et de gérer les risques. Une gouvernance à 5 comme cela a été le cas dans le processus français « Grenelle de l'environnement » décidé par la Présidence de la République française en 2007 peut contribuer activement au chapitre 4 Opinion du SCENIHR : les intérêts communs des 5 parties peuvent faire émerger des mesures immédiates et négociées pour développer les connaissances, identifier et maîtriser les risques environnementaux et sanitaires liés à des pollutions d'un nouveau type, incluant les nanomatériaux. Dans le cadre de ce processus qui a mis en place le travail a été effectué en constituant des collèges qui avaient pour vocation de représenter les acteurs du développement durable : ? l'Etat et divers de ses établissements publics, ? les collectivités territoriales et les parlementaires, ? les associations de protection de l'environnement et plus largement ONG de protection de l'environnement, ont été associées aux travaux avec voix consultative les associations représentants les intérêts des familles et des consommateurs, ? les employeurs, ? les représentants de travailleurs. Le thème nanotechnologies a donné lieu à des décisions, y compris la consultation de la Commission nationale du débat public pour organiser un débat public qui aura lieu en automne 2009, notamment dans 18 villes de France. Ce qui prouve l'efficacité de cette démarche à 5. D'ores et déjà des scientifiques élaborent des présentations claires compréhensibles par des citoyens sans culture scientifique développée pour alimenter ce débat : ils voient donc que leur rôle pédagogique au sein de la société est réel et peut conduire à des choix responsables. Le SCENIHR n'identifie pas l'intérêt d'une alerte rapide. La

Commission européenne a créé un groupe interservices consacré à tous les aspects des travaux décrits dans le rapport « plan d'action » et la création d'un observatoire devrait s'inspirer d'une gouvernance à 5 pour faciliter l'identification et la gestion des risques des nanotechnologies. La fédération France Nature Environnement souligne que le système d'alerte rapide pour les institutions communautaires et les États membres est urgent : le rapport du SCENIHR est suffisamment clair sur les risques potentiels et actuels. Cette alerte implique de mesures concrètes et immédiates, qui doivent inclure si nécessaire un arrêt de mise sur la marché en attendant confirmation de l'innocuité (dit « moratoire » en français) et un étiquetage précis. Bien évidemment pour qu'une telle gouvernance puisse fonctionner il faut que l'ensemble des représentants des parties prenantes puisse accéder aux informations. Dans un contexte des nanotechnologies, la construction de nouvelles formes de gouvernance devient incontournable, les mécanismes habituels de la gestion des risques fondés sur une négociation impliquant les producteurs, les experts et les autorités, ne suffisant plus. S'appuyer sur des formes innovantes de participation de la société civile, qui soient susceptibles de contribuer à fonder la confiance des différents acteurs concernés, peut véritablement contribuer au renouvellement des formes traditionnelles de participation et de débat public en matière de santé environnementale et humaine. Un modèle itératif de prise de décisions doit être utilisé, s'inscrivant dans l'esprit de la convention d'Aarhus (de juin 1998). Il faut donc : o mettre en place un espace de concertation dédié, o impliquer les parties prenantes, la gouvernance à 5, o promouvoir une certaine forme d'équité entre les parties et donc donner aux associations les moyens adaptés. Pour produire des décisions acceptables, FNE demande de : - remettre un ensemble de valeurs au cœur du débat et pas uniquement celles de la compétitivité et de l'importance des marchés, - avoir pour objectif de prendre des décisions économiquement, écologiquement et sociologiquement acceptables.

References Nanosciences et nanotechnologies: un plan d'action pour l'Europe 2005-2009. Premier rapport de mise en oeuvre 2005-2007

Submission: 42

Organisation Fédération France Nature Environnement

Type NGO

publishing Yes

Comments Absence d'évaluation par le SCENIHR des risques liés à un manque de moyens d'information sur ce qui est commercialisé. Si les nanotechnologies suscitent une telle méfiance d'ordre toxicologique de la part des ONG, c'est que les études actuelles indiquent clairement l'existence de risques environnementaux et sanitaires et le rapport SCENIHR du 19 janvier 2009 les confirme. Les paragraphes Human exposure et environmental exposure du chapitre 4 sont particulièrement pertinents et soulignent l'absence de possibilité d'évaluation des risques par manque d'information sur les produits commercialisés ; les conclusions n'en sont malheureusement pas tirées. 1. La déclaration obligatoire pour identifier et réduire les risques Dans le cadre d'un projet de loi en cours d'adoption par le Parlement français il est prévu que « L'État se donne pour objectif que, dans un délai de deux ans qui suit la promulgation de la loi, la fabrication, l'importation ou la mise sur le marché de substances à l'état nanoparticulaire ou d'organismes contenant des nanoparticules ou issues de nanotechnologies fasse l'objet d'une déclaration obligatoire, relative notamment aux quantités et aux usages, à l'autorité administrative ainsi qu'une information du public et des consommateurs. » Cette mesure devrait être étendue à l'Union Européenne dans les meilleurs délais compte tenu des besoins d'information des scientifiques. 2. L'étiquetage pour prévenir le risque de consommation contre indiquée La fédération France Nature Environnement tient à souligner que l'absence d'étiquetage précis de produits franchissant les barrières biologiques pour atteindre organes, tissus, noyaux des cellules et interférant avec l'ADN du monde végétal et animal est irresponsable et incompréhensible, compte tenu des règles actuelles européennes d'étiquetage des produits quelque que soit leur degré établi de dangerosité. Même les colorants figurent sur la liste des ingrédients : pourquoi pas les nanoparticules ? Cet étiquetage évitera le risque de consommer des produits contre indiqués pour des raisons médicales ; et les scientifiques

disposeront enfin d'éléments pour estimer les expositions probables. Sur un plan éthique, cette démarche parait aussi indispensable. Les chiffres d'affaires générés par la commercialisation des nanoproduits permettent de mettre en place des moyens d'étiquetage satisfaisants, avec communication tant aux agences sanitaires européennes qu'au public par la mise en ligne d'information comme elle se pratique aux USA. Un étiquetage détaillé permettra aussi aux scientifiques d'avoir une information nécessaire sur les caractéristiques des nanoproduits mis sur le marché et compléter leurs bases de données. Pour FNE toute mise sur le marché européen de nanoproduits doit, dans les plus brefs délais, à l'instar du modèle américain s'accompagner d'une étiquette détaillée comprenant au minimum : la taille des particules, la concentration en nanoparticules, la structure des particules et du substrat, la nanotechnologie utilisée, la classification (exemple colloïde). Lors de discussions entre parties prenantes en France, cette étiquette a permis enfin de prendre des exemples concrets (colloïde d'argent) et de poser des questions pertinentes sur l'innocuité du produit, son utilisation potentielle, etc. Tant qu'il n'y aura pas d'étiquette claire, les débats resteront théoriques, les risques incertains et les responsabilités de chacun ne pourront pas être assumées. FNE demande : ? Qu'avant 2010 tout produit à usage alimentaire ou cosmétique, contenant des nanoparticules et mis sur le marché, soit soumis à un étiquetage adapté ; ? Qu'à partir de 2010 tout produit contenant des nanoparticules et commercialisé dans un circuit grand public ou professionnel (y compris sous traitance) soit soumis à un étiquetage adapté ; ? Que la déclaration produit contienne des informations les plus exhaustives possibles et soient accessibles sur le net.

References Projet de loi français : « Le projet de loi de programmation relatif à la mise en œuvre du Grenelle de l'environnement » Au 14/06/2009 en cours d'adoption par le Parlement français (en 2ème navette) Une fois adoptée et publiée, la loi sera consultable : http://www.legifrance.gouv.fr Des informations selon le modèle américain : http://www.nanotechproject.org/process/assets/files/7039/silver_database_fauss_sept2_final.pdf

Submission: 43

Organisation Fédération France Nature Environnement

Type NGO

publishing Yes

Comments Absence d'identification par le SCENIHR de moyens de vigilance et de surveillance, à tous les stades du cycle de vie du produit Si les dangers d'exposition sanitaires et environnementaux sont bien explicités la nécessité d'une mise en place de moyens de vigilance et de surveillance, à tous les stades du cycle de vie du produit est absente : elle permettrait à la fois de réduire au maximum l'exposition aux risques et de fournir aux scientifiques des éléments d'étude. 1. La fédération France Nature Environnement demande aux autorités de mettre en place un ensemble de mesures sur les processus industriels : - Prévoir la surveillance des installations de toute nature fabricant ou utilisant des nanoparticules par les représentants de l'Etat qui ont la mission de surveillance et contrôle des rejets des activités économiques, - Mettre en place, en matière de nanoparticules, des dispositifs de surveillance de l'air ambiant et de l'air intérieur et des eaux de surface à proximité de ces installations, - Recenser les filières de production, d'utilisation et d'élimination des nanoparticules, - Former les médecins du travail et les services d'intervention d'urgence : procédures et protections individuelles pour les sauveteurs amenés à intervenir dans des atmosphères contaminées, procédures pour traiter les victimes, - Inventorier et rendre accessible au public la liste des nanomatériaux commercialisés ou en voie de l'être de même que les produits en contenant avec leurs caractéristiques. 2. Il est essentiel que les déversements de nanoparticules / nanomatériaux dans les milieux (eau, air, sols) soient interdits dans les plus brefs délais avant que les taux de nanoparticules ne soient suffisamment élevés pour être mesurables. FNE souligne que le but n'est pas de laisser les milieux absorber assez de nanoparticules pour servir de champs d'expérience et valider des hypothèses scientifiques. Les retours d'expériences en qualité de l'air pour des particules de tailles supérieures montrent depuis longtemps les difficultés de dépollution auxquelles la planète est confrontée. Actuellement aucune étude de faisabilité de dépollution n'existe sur les nanoparticules et encore moins sur les coûts. 3. FNE demande que les productions soient développées

en intégrant la notion de risques et que l'UE rende obligatoire : - sur site industriel des instruments de mesure adaptés indiquant la présence et / ou la concentration en nanoparticules, pour savoir dans quelles conditions une intervention spécifique est nécessaire ; - la mise en place des modes de gestion des résidus et rejets de production afin d'exclure toute dispersion de nanoparticules dans les milieux ; - l'accompagnement de tout programme de développement de nouveaux produits de tests portant sur leur innocuité, notamment par des tests sur cellules, la communauté internationale mettant en doute l'intérêt de tests systématiques sur animaux. Il est urgent que des moyens financiers suffisants, cohérents avec les investissements industriels, soient consacrés à la prévention des risques : le SCENIHR soulignant les risques transgénérationnels dus aux nanoparticules et nanomatériaux, l'engagement de l'Union européenne vis-à-vis du développement durable, implique d'inclure ces recommandations. Le plan d'action ambitieux de l'UE ne sera envisageable qu'avec des recommandations fortes sur les points soulignés par FNE.

References Nanosciences et nanotechnologies: un plan d'action pour l'Europe 2005-2009. Premier rapport de mise en oeuvre 2005-2007

Submission: 44

Organisation Fédération France Nature Environnement

Type NGO

publishing Yes

Comments Absence de prise en compte par le SCENIHR des risques d'exposition des travailleurs et sécurité au travail En raison des dangers d'exposition décrit dans le rapport du SCENIHR, la fédération France Nature Environnement demande que soient mis en œuvre rapidement un ensemble de mesures au profit des travailleurs. 1. Le SCENIHR n'a pas traité les risques de manipulation sans information suffisante et donc le danger d'exposition par ignorance. Les travailleurs des secteurs concernés, fabricants, utilisateurs de nanoparticules ou /et de nanomatériaux, réparateurs de produits et matériaux en contenant, vont être de plus en plus nombreux dans les mois et années à venir. Ils doivent bénéficier d'un ensemble de mesures de prévention et de précaution : ? En tout premier lieu, ils doivent bénéficier d'informations et de formations, sur les risques éventuels, sachant que les risques d'explosion des certains nanomatériaux existent. ? L'étiquetage lisible et apparent est un élément essentiel du dispositif, la traçabilité étant nécessaire à tous les stades de manipulation et de transformation, de stockage et d'élimination. ? Les travailleurs doivent aussi bénéficier de la prise en compte de cette exposition dans le cadre de la surveillance médicale dont ils bénéficient. ? Les médecins du travail doivent être formés aux risques spécifiques des nanoparticules et nanomatériaux. Enfin cet aspect de risques sanitaires pour les travailleurs doit être intégré, à l'échelle européenne, dans le cadre d'une surveillance sanitaire sous forme de cohorte. L'OSHA, European Agency for Safety and Health at Work, pourrait être parmi les acteurs de formation et d'information impliqués. 2. Les risques d'intervention des personnels de secours et de traitement des victimes ne sont pas identifiés. ? Les services d'intervention d'urgence doivent être formés aux risques spécifiques des nanoparticules et nanomatériaux. ? Les procédures et protections individuelles pour les sauveteurs amenés à intervenir dans des atmosphères contaminées par les nanoparticules et nanomatériaux, et donc ils doivent avoir connaissance de la liste des établissements qui utilisent ces matériaux. ? Les procédures pour les hôpitaux devant traiter les victimes soumises à des taux élevés de nanoparticules doivent être adaptées.

References European Agency for Safety and Health at Work http://osha.europa.eu/en/riskobservatory/teaser/nanotechnologies European civil protection http://ec.europa.eu/environment/civil/index.htm

Submission 45 : withheld upon request of the author

Submission: 46

Organisation Dr Hadwen Trust For Humane Research

Type NGO

publishing Yes

Comments Although recent reports have highlighted issues arising from nanomaterials and their impacts, particularly regarding insufficient knowledge and data regarding toxicology, we feel one key area has been neglected, possibly leading to increased risk that could result from the use of nanomaterials. At the Dr Hadwen Trust we believe the lack of adequate safety testing in the field of nanomaterials will impact dramatically on animal testing and forms a central component of the debate on their risks. It is of central concern to the Dr Hadwen Trust that existing animal-based safety tests are being used to assess nanomaterials, even though their applicability has never been established and, furthermore, has been questioned on numerous occasions including by the Commission's own scientific advisors. It is certainly possible, and may even be assumed to be likely, that conventional animal tests cannot be relied upon to identify the potential of nanomaterials to produce toxic effects in human beings. Thus animal welfare is compromised because animals are used in painful toxicity tests, and human health is compromised because the animal tests are not able to provide regulators or companies with relevant or reliable safety data. Whilst the EU is funding the development of some non-animal tests for nanomaterials, it is unlikely that all of these will be ready in the immediate future for all the toxicity endpoints. However, the same can be said for animal tests. Where statements are made about the lack of availability of non-animal methods, we would expect to see a matching acknowledgement that existing animal tests are not validated for this application. There are basic nanomaterial-specific scientific problems related to in vivo experimentation. Challenges related to tracking nanoparticles in vivo and delivering a relevant dose to animals presents practical problems that affect each test performed in animals. The large diversity of nanomaterials results in an exponential increase in the actual numbers of differing nanoparticles and in the impracticality of using animals due to time, costs and animal numbers. For many parameters there is no adequate, scientifically robust testing procedure and considering the variability that can exist between nanomaterial preparations and even between the same nanomaterial preparations tested at different times, together with the absence of a 'universal' nanomaterial form of any individual substance it is scientifically dubious to continue with current testing procedures. According to scientific research the health risk of nanomaterials depends on many more factors than the ones normally taken into account in safety assessments; small particle size producing systemic exposure and toxicity, surface affects, particle size affecting external and internal exposure parameters, physical shape and charge. Without established definitions for nanoparticles taking into account the substantially different properties apparent from nanoparticles of the same substance but produced by different manufacturers, it is impossible to rely on safety data produced using conventional assessment methodologies. At the Dr Hadwen Trust we therefore see the priorities for research centering on the development of nano-specific non-animal testing strategies and the implementation of a tired testing approach employing a battery of in-vitro test methods and a tiered, weight-of-evidence approach that is based on the most relevant methods available at this time. There are indeed a number of non-animal techniques currently being developed that represent a potential methods. Companies should submit data using those methods, so that applicable data on each nanoform can be assessed, and useful comparisons can be made so as to assess durability and possible changes in toxic properties over time. Irrelevant animal data should not be used to mask the uncertainties associated with nanoparticle use.

References Hoehr D, Steinfartz Y, Schins R et al (2001) The surface area rather than the surface coating determines the acute inflammatory response after instillation of fine and ultrafine TiO2 in the rat. Int. J. Hyg. Environ. Health 205;239-244 Lockman P, Koziara J, Mumper R, Allen D (2004) Nanoparticle surface charges alter blood-brain barrier integrity and permeability. Journal of drug targeting 12;635-641 Warheit D, Reed K, Webb T (2003) Pulmonary toxicity studies in rats with triethoxyoctylsilane (OTES)-coat pigment-grade titanium dioxide particles: bridging studies to predict inhalation hazard. Exp Lung Res 29;593-606 Wahrheit D, Webb T, Reed K et al (2006) Pulmonary toxicity study in rats with three forms of

ultrafine-TiO2 particles: Differential responses related to surface properties. Toxicology 230;90-104 Wahrheit D, Hoke R, Finlay C et al (2007) Development of a base set of toxicity tests using ultrafine TiO2 particles as a component of nanoparticles risk management. Toxicology letters 171;99-110 Ng, C and Pun, SH (2007) A perfusable 3D cell-matrix tissue culture chamber for in situ evaluation of nanoparticle vehicle penetration and transport. Biotechnology and Bioengineering 99:1490–1501. www.hurelcorp.com

Submission: 47

Organisation Proefdiervrij (Dutch Society for the Replacement of Animal Testing)

Type NGO

publishing Yes

Comments Nanotechnology: Threats to Laboratory Animals Animal testing is currently taking place in order to investigate the health effects of nanoparticles. It is a proven fact that some nanoparticles are harmful. Examples are asbestos and carbon black in printer toners. Safety evaluation of nanotechnology products differs from present-day risk assessments. As well as the amounts of substance taken in by the body (expressed in weight), other factors of importance in nanotechnology are the shape, the surface properties and the size of the nanoparticle. Hence, different testing methods are required. But why start with animal testing, only to replace those tests later with methods sparing laboratory animals? The Dutch Society for the Replacement of Animal Testing (Proefdiervrij) believes that available research data on nanoparticles collected through animal testing should be shared by companies, so as to avoid duplication of testing. Nanotechnology: An Opportunity to Replace Animal Testing Experience has demonstrated that animal testing is full of constraints and incurs high costs. This kindles the demand for more methods not involving laboratory animals. Nanotechnology offers us a great opportunity. Animal testing must be limited, whereas patient and consumer safety must be guaranteed. In order to attain this, the first priority is to validate screening tests which do not involve laboratory animals. Because toxicity testing of nanoparticles is still at a developing stage, scientists should focus on methods not involving animals. Cooperation between nanotechnologists and toxicologists, for example, would enable them to gain insight into the possible detrimental effects of nanostructures at an early stage. The Position of the Dutch Society for the Replacement of Animal Testing (Proefdiervrij) Naturally, the Dutch Society for the Replacement of Animal Testing opposes animal testing. That is the very reason we were established in 1897. But we are not against health, nor against safety. Medicine must cure, without nasty side effects. And our detergents should not cause irritation, or harm the environment. All too often, when investigating new materials or technologies, we revert to the old and trusted methods of animal testing. It is no more than an intermediate step, and it does not eliminate all the risks subject to investigation. The Dutch Society for the Replacement of Animal Testing is of the opinion that this step in the process needs to be replaced. Nanotechnology opens up excellent opportunities for a pilot. The aim is to ensure human, animal and environmental safety, without carrying out experiments on animals. If this proves possible, then, for sure, wider applications are also within reach. In order to achieve this, additional resources need to be invested in methods not involving laboratory animals. Not only scientists and politicians must be made aware of this, but the public at large. An example is the initiative by Unilever called Assuring Safety without Animal Testing (ASAT). The ASAT programme is designed to protect human and environmental health through sustainable and transparent means. The programme uses models which guarantee the safety of chemical products. It is expected that the application of these methods will eventually be extended to other fields. The Dutch Society for the Replacement of Animal Testing petitions for the development of techniques which do not involve laboratory animals, in order to investigate the effects of nanotechnology. Why invent testing strategies on animals first, only to replace them later? We believe it is high time for non-animal test methods.

Submission: 48

Organisation Food Safety Authority of Ireland

Type Public authority

publishing Yes

Comments My submission is more general than scientific in detail. Coordinated laboratory work should begin immediately on characterising the risks posed by certain nanomaterials while such evaluation should be prioritised based on exposure levels. Products made from, or containing nanomaterials already on the market should be examined as a priority. All products for evaluation should be graded with regard to potential for human exposure to nanoparticles. For example, packaging from which nanomaterials do not migrate would be of lower priority than foods containing engineered nanoparticles where human exposure is guaranteed. Products containing engineered nanoparticles should take priority over naturally occurring or organic nanoparticles. No standards are yet in place for the risk assessment of nanomaterials and as the risk to human health are largely unknown as yet the precautionary principle should prevail. Standard processes designed for other areas must be used with caution in the risk assessment of nanoparticles. In-vitro studies should be used in the initial characterisation from which information can then be fed into a process which would determine whether there is a need to progress to in-vivo studies or not. The frontline use of in-vivo studies is no longer necessary or acceptable except, for example, where a screening process indicates a need. While long term studies are necessary, they should share priority with, and be carried out alongside efforts to determine any acute impacts on human health. Data on products containing nanomaterials already on the market should be collected as a priority to determine whether any current health problems can be linked to the use of these nanomaterials.

Submission: 49

name Dr. Enrique Navarro Rodríguez

Individual

publishing Yes

Comments ASSESSING ECOTOXICOLOGICAL IMPACTS OF NANOMATERIALS REQUIRES A COLLABORATIVE EFFORT BETWEEN ECOTOXICOLOGISTS, CHEMISTS, PHYSICISTS AND NANOTECHNOLOGIES DEVELOPERS AND COMPANIES Nanotechnology-related applications are expected to have an impact of billions of Euros and millions of jobs during the next decade. This unique opportunity for economic growth needs to be supported by a strong parallel effort on the hazards and risks of these materials, so that concerns about the environment or human health do not undermine public confidence in this new technology. Because many applications of nanomaterials (NM) are in an early phase of development and implementation, we should take the opportunity to develop tools to prevent, reduce or avoid the drawbacks of this promising technology [1]. Risk assessment needs both an appropriate knowledge of NM effects and realistic exposure assessment for relevant organisms; at present, knowledge gaps in these two fields prevent adequate NM risk assessment. One major concern is that the novel physicochemical properties of NM are incompatible with our current standard toxicity testing protocols. As has been stated by the Scientific Committee on Emerging and Newly Identified Health Risks of the EU [2], “although the existing methods are appropriate to assess many of the hazards associated with the products and processes involving nanoparticles, they may not be sufficient to address all the hazards”. From recent reviews on the hazard and environmental risk of NMs [3-9] some common features have emerged. First, that there are not enough experimental data to support risk assessment [2]. Only a few quantitative analytical techniques for measuring NM in environmental samples are available, which results in a serious lack of information about their occurrence in the environment [10-12]. Often the

available data use a limited number of test species (e.g., standard OECD test organisms) and NM, along with potential flaws in standard protocols when applied to NM. Second, there are many groups of organisms, even whole phyla, for which data are absent and we are a long way from “protecting all organisms most of the time” from NM. Third, consensus has not been reached on exactly what aspects of particle characterization, or types of particle controls, should be included in order to make a “good” experiment on hazard. This research must be multidisciplinary so that the scientific community normally involved in risk assessment (i.e., ecologists, ecotoxicologists and environmental chemists) is engaged with the nanotech community (e.g., engineers, physicists, material scientists). Otherwise, important aspects related to the characterization of NM in relevant media, or possible novel mechanisms of toxicity, may be overlooked. Therefore, a framework at European level is required allowing interactions between ecotoxicologists, chemists, physicists and nanotechnology-developers and firms that apply these nanomaterials in consumer products. Such collaborations, in parallel with the development of a nanomaterial or its applications, are expected to benefit all partners by ensuring that information about biological interactions of such materials is available for technology developers. These data will be useful for both reducing future impacts in the environment (and helping consumer products through future registration processes, e.g. under REACH), and also for identifying promising characteristics that can be enhanced for other purposes in the future (e.g., new biocides). Furthermore, basic knowledge will arise from such multidisciplinary collaborations, specially identifying NM properties and mechanisms provoking toxic effects on organisms. At present, there is an ongoing proposal called EuroNanoEcotox (it is a ESF-EUROCORES Theme), which aims at providing such framework.

References

1. Hansen, S.F., et al., Late lessons from early warnings for nanotechnology. Nature Nanotechnology, 2008. 3(8): p. 444-447. 2. SCENIHR, The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies. 2005, European Commision, Directorate C - Public Health and Risk Assessment. p. 79.Available from: http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003b.pdf 3. Farre, M., et al., Ecotoxicity and analysis of nanomaterials in the aquatic environment. Analytical and Bioanalytical Chemistry, 2009. 393(1): p. 81-95. 4. Klaine, S.J., et al., Nanomaterials in the environment: Behavior, fate, bioavailability, and effects. Environmental Toxicology and Chemistry, 2008. 27(9): p. 1825-1851. 5. Tsuji, J.S., et al., Research strategies for safety evaluation of nanomaterials, part IV: Risk assessment of nanoparticles. Toxicological Sciences, 2006. 89(1): p. 42-50. 6. Nel, A., et al., Toxic potential of materials at the nanolevel. Science, 2006. 311(5761): p. 622-627. 7. Moore, M.N., Do nanoparticles present ecotoxicological risks for the health of the aquatic environment? Environment International, 2006. 32(8): p. 967-976. 8. Dowling, A., et al., Nanoscience and nanotechnologies: opportunities and uncertainties., S.P. Section, Editor. 2004, The Royal Society & The Royal Academy of Engineering: London.Available from: http://www.nanotec.org.uk/finalReport.htm 9. Navarro, E., et al., Environmental behavior and ecotoxicity of engineered nanoparticles to algae, plants, and fungi. Ecotoxicology, 2008. 17(5): p. 372-386. 10. Nowack, B. and T.D. Bucheli, Occurrence, behavior and effects of nanoparticles in the environment. Environmental Pollution, 2007. 150: p. 5-22. 11. Hassellov, M., et al., Nanoparticle analysis and characterization methodologies in environmental risk assessment of engineered nanoparticles. Ecotoxicology, 2008. 17(5): p. 344-361. 12. Tiede, K., et al., Detection and characterization of engineered nanoparticles in food and the environment. Food Additives and Contaminants, 2008. 25(7): p. 795-821.

Submission: 50

name Roger Stimson

Individual

publishing Yes

Comments I have a simple question, which may, however be an entirely new concept in innovation. If there is no serious problem expected from the use of nanotechnology, why would it not be possible and also intelligent to discover and create an 'antidote' or restoration potential to each aspect of expected application before releasing the active aspect of the science?

Submission: 51

name Dr Athanassios E. Tyrpenou, DVM, MSc, PhD Food Hygienist

Individual

publishing Yes

Comments 1. As previously discussed, when measuring nanoparticles in different media, it is not only necessary to generate data on concentrations but information will also be required on the size distribution and properties of the particles. 2. Moreover, while a range of methods have been shown to be applicable to the analysis of nanoparticles, the current methods do not fulfill all data requirements. 3. In complex media, it is essential to analyze samples of diverse elemental compositions and samples containing more than one type of nanoparticle. Many techniques are destructive or, if not, application of some sample preparation methods can lead to artifacts. 4. There are many methods available for the sizing of particles, but very few, if any, is applicable to the entire size range. 5. Analytical methods are required to reliably detect and characterise nanoparticles and their properties in matrices to which humans and ecosystems are exposed, including air, soil and water as well as food and consumer products (SCENIHR 2005). 6. These techniques have to be able (a) to deal with heterogeneous samples, (b) minimize sample alteration to avoid artifacts and (c) provide as much information as possible, because most characterization techniques are destructive and, therefore, samples often cannot be analyzed twice or by more than one technique. 7. The existing tools do not fulfil all desirable criteria and have limitations when considering their application for food and natural samples. Therefore, until new tools have been developed, existing tools have to be used and combined in such a way that data can be validated. 8. Nanotoxicology and nanoecotoxicology are still in their infancy and risk assessments are practically nonexistent, especially in the food sector. Therefore, progress in nanoparticle testing (in vivo and in vitro) is urgently needed to guarantee consumer safety, including the development of standard testing materials and testing guidelines. In addition to toxicity studies, various uptake paths have to be studied, including dermal, oral and intestinal, as well as nanoparticle accumulation and potential long-term effects. 9. Other effects of nanoparticle uptake could be the interaction with other (toxic) substances and their mobilisation or dislocation, not only in the human body, but also in consumer products. The environmental fate, behaviour and bioavailability of nanoparticles is unknown and, thereby, their potential impact on food webs and persistence. 10. Furthermore, data on environmental and exposure concentrations are unavailable. Developments in the above-mentioned analytical fields will be crucial to further our knowledge of nanoparticle and related issues. SO, AFTER ALL THESE INCOHERENCE CONCERNING ALL SAFETY ISSUES OF NANOTECHNOLOGY IN FOOD AND FEED IT IS ABSOLUTELLY IMPERATIVE NANOTECHNOLOGY NOT TO AUTHORISED FOR FOOD AND FEED AND IT IS URGENTLY PREQUISITE TO CHECKED IN DEPTH FOR HUMANS, ANIMALS, PLANTS AND ENVIRONMENT FUTURE PROTECTION.

References Detection and characterization of engineered nanoparticles in food and the Environment Karen Tiede; Alistair B. A. Boxall; Steven P. Tear; John Lewis; Helen David; Martin Hassellöv Food

Additives & Contaminants: Part A, 25:7,795-821, 2008 The EFSA Journal (2009) 958, 1-39 SCIENTIFIC OPINION-The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety1. Scientific Opinion of the Scientific Committee (Question No EFSA-Q-2007-124a) Adopted on 10 February 2009

Submission: 52

Organisation Swiss Federal Office of Public Health (FOPH)

Type Public authority

publishing Yes

Comments The "Opinion on risk assessment of products of nanotechnologies (2009)" of the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)1 summarizes, confirms and even enlarges the knowledge presented in the preceding SCENIHR opinions. The opinion provides an excellent and comprehensive overview of the state of the art regarding "hazard identification" and "exposure estimation", including an up-to-date inventory of existing tools for assessments such as the SCENIHR algorithm, expert judgement matrix or even the Swiss Precautionary Matrix. It also identifies the knowledge gaps regarding these issues and indicates what has to be done to overcome these gaps. Nonetheless, it has to conclude that these uncertainties probably will remain for some time until there is sufficient scientific information available.

Therefore, a question yet to be asked in the hearing is what kind of risk assessment and related precautionary measures can support industries and research institutes in minimizing the risks under uncertainty while taking decisions for innovation trajectories.

Public agencies, industry and researchers have to deal with these uncertainties. For public agencies it is a challenge to address the needs of the different stakeholders. For one thing, this is mainly due to wide gaps in scientific knowledge and for another to the continual emergence of new knowledge, thus causing a need for ongoing adaptation in risk assessment approaches for engineered nanomaterials (ENM)2 (a "moving target", Laursen 2008). Furthermore, the market for new nanoproducts is evolving fast and the scientific knowledge on the risks involved is lagging.

Nanotechnologies comprise a wide area of industrial sectors and scientific disciplines. According to our experience the situation for innovation in the field of nanotechnologies in industry and research is determined by the following issues:

- "new" sectors and scientific disciplines may be involved, where the assessment and handling of potentially hazardous substances is not yet established (Schmid et al. 2008)
- SME's and material scientists have neither the personnel nor the time to observe in detail the evolving knowledge in the area of risk assessment.
- the knowledge of the risks posed by nanomaterials is often fragmented and published in very detailed form. Comprehensive overviews concerning state of knowledge concerning opportunities and unintended side-effects for certain ENM and specific applications are not available.

Driven by the experiences we have gained when addressing these challenges in Switzerland, we wish to contribute to the public consultation for the "Scientific Hearing on Nanotechnology" by highlighting issues of major importance for the field of safety in nanomaterials. In our comments we will focus on how risk assessment of nanomaterials should be enhanced in order to allow a "safe, integrated and responsible" development of nanotechnologies through a discussion of the following topics:

- the Swiss approach to complement current risk assessment tools by applying the precautionary principle, based on scientific grounds, in order to support industry and commerce as well as research institutes in making informed decisions for sustainable innovation in the field of nanotechnologies: the Swiss Federal Office of Public Health (FOPH) and the Federal Office for the Environment (FOEN) have

launched, in the frame of the "Swiss Action Plan Synthetic Nanomaterials" 3, a "Precautionary Matrix for Synthetic Nanomaterials"

- methodologies of exposure assessment that may provide valuable information for the enhancement of the risk assessment
- the value of the life cycle concepts in the framework of prospective technology assessment, which provide information for exposure assessment and an integrated and prospective view of the risks of nanotechnologies.

1 SCENIHR, Opinion on risk assessment of products of nanotechnologies, 19 January 2009.

2 The term "engineered nanomaterials"(ENM) is used in this report as a collective term for "nanoparticles", "nanorods", "nanoplates" (discrete pieces of material with one or more external dimensions in the nanoscale).

3 Available from: URL: http://www.bafu.admin.ch/publikationen/publikation/00574/index.html?lang=en

1 Identification of possible topics not yet covered

1.1 Practicable tools for implementation of Precautionary Principle

Most of the currently available tools for risk assessment are not made to be used in a wide range of industrial fields or by stakeholders. Some approaches exist to address the assessment of nanotechnological risks, as exemplified in chapter 3.7 of the recent SCENIHR opinion. Even if the approaches are logical and objective, they are usually not understandable or practicable for use by most stakeholders, who urgently need such a tool, namely industries (especially SMEs) and researchers. There is a gap in the availability of ready-to-use tools to be implemented by industry or research. Thus, no tools have been made available for direct use. In order to overcome this bottleneck, a Precautionary Matrix has been initialised and launched by Swiss Federal Office of Public Health (FOPH) and the Federal Office for the Environment (FOEN) in Switzerland. Since its first publication in 2008 (the form in which it is mentioned in the SCENIHR Opinion) it has been further developed in close collaboration with the industry, and now it has a stronger focus on identifying gaps or hotspots in current knowledge, and on fostering actions and measures to be taken accordingly. In the currently ongoing process of evaluating and improving the practicability of the Matrix, an electronic version of the Matrix with an automated analysis of the input has been developed. This version will presumably be available end of 2009.

Therefore, a topic additionally to be covered is the way the Precautionary Matrix is supposed to work now. As a very important clarification it should be mentioned that the Matrix is by no means a risk assessment tool, but a screening device for possible risks, which cannot yet be quantified. In order to preclude any erroneous perception of the possible output of the Matrix, a public discussion would be highly beneficial on the overall concept of the Precautionary Matrix to address stakeholders' needs.

Some of the basic concepts used in the Precautionary Matrix, originating from numerous discussions with Swiss scientific experts could be added to the discussion in an advantageous way:

- even if agglomerated nanoparticles may be much larger than the borders defined for engineered nanomaterials, deagglomeration may occur in physiological or environmental conditions, and should thus be looked at in any assessment approach
- apart from changing physico-chemical properties when entering the nanoscale, a discussion of particles with sizes up to 500 nm should be taken into account. This is due to possibly changed interactions with the biological surrounding as a pure size effect independent of physico-chemical properties (e.g. the size limit for macrophages to scan foreign bodies is around 500 nm)
- within the frame of the Precautionary Matrix it is assumed that the main source of concern for health and the environment is only with nanoparticles (3 dimensions on the nanoscale) and nanorods (2 dimensions on the nanoscale).

Short overview of the concept

The precautionary matrix estimates the risk potentials – throughout the whole life cycle – for the health of workers and consumers, and for the environment.

The precautionary matrix is based on a limited number of evaluation parameters. The potential effect is estimated by the reactivity and stability of the engineered nanoparticles (ENP). The probability and degree of exposure of human beings and input into the environment are examined through data on the physical surroundings of the ENP, the amount marketed and the emission of ENP from production or use.

The precautionary matrix is made up of modules for these evaluation parameters. This structure ensures that new scientific information on effects, the exposure of human beings or inputs into the environment can be taken into account at any time.

1.2 Exposure assessment

The risk is determined by the potential hazard of ENM and the exposure to ENM (Risk = Hazard x Exposure). Assessments of environmental and human exposure to ENM are still rare in comparison to assessments of unintended effects on human health and the environment. SCENHIR (2009) describes the state of the art of methodologies measuring ENM for occupational health exposure, both in different environmental compartments (air, water, soil) and in products, and the methodological deficiencies.

From this perspective, methodologies for environmental exposure modelling, human exposure assessment (consumer exposure) and experiments on the release of ENM from nanoproducts should be intensively addressed and refined.

Environmental exposure modelling

Three important aspects of the exposure assessment that need to be closer examined are:

- the total amount of ENM produced and used
- the release of ENM during the production, use and disposal of products
- the development of analytical methods to measure ENM in natural systems

Thus far these aspects have received much less attention than ENMs' environmental behaviour, however, they are essential for conducting an exposure modelling of ENM in the environment. Details of the actual usage of ENM in products, production amounts and forms of ENM in products (morphology, size, functionalisation) comprise the most basic information that is absolutely necessary for any risk assessment. However, this information is almost completely missing. Initiatives such as the Swiss "NanoInventory" (Schmid et al. 2008)" are needed on a European basis to get quantitative information on the production of ENM. Because the life cycle of the nano-products determines when and where ENM can be released, it is also of paramount importance to have quantitative information on the usage of nano-products and the quantities, type and form of the used ENM in these products. Thirdly it is necessary to get quantitative data about the release of the ENM from these products during use and disposal, and also during production of the ENM and the nano-products. In these studies not only the quantity of the released ENM but also the form needs to be studied. Almost all ecotoxicological and environmental fate studies so far have been conducted with pure, pristine ENM. However, the particles that are released from actual products may have completely different properties, e.g. different coatings, or may have been changed by aging. Future ecotoxicological and environmental fate studies need to work with actually released particles if research shows that these particles have properties different from the normally used pristine particles.

An important step in validating modelling studies and a prerequisite for realistic environmental fate and release studies is the development of trace analytical techniques for ENM in natural matrices. Significant improvements and new approaches for both inorganic and organic ENM are needed. It is necessary that these methods are able to measure ENM in wastewater and sludge and at trace concentrations also in natural waters, in soils receiving sewage sludge and in sediments. These methods should preferably also be able to distinguish between different functionalizations and yield information on natural surface coatings.

The data obtained by taking the approaches listed above should enable one to refine the current exposure modelling of ENM.

Analysis of human exposure (consumer exposure)

The market for products made of nanomaterials is emerging quickly. Consumer exposure due to new retail products containing or consisting of nanomaterials may be expected. However, it remains basically unclear what kind of exposures and magnitudes of exposure may be reached in the near future. The Swiss Federal Office of Public Health (FOPH) is funding a project that aims to assess consumer exposure to engineered nanoparticles (ENP) resulting from intended, direct usage of market products. It distinguishes among dermal, oral and inhalation exposure for several consumer groups, differing in gender and age. The project focuses on the

product categories where ENP today are most frequently found and toxicologically of the most concern: textiles, cosmetics & personal care products and household sprays.

The project includes firstly data collection through literature research and experimental analysis of the release of ENP from products, and secondly exposure modelling on the basis of the data collected. The results of the project represent a valuable source of exposure data, which - combined with toxicological data - can be taken as a basis for a systematic risk assessment, hence supporting the development of safe and sustainable consumer products. (http://www.sust-chem.ethz.ch/research/groups/exposure_analysis)

Release of ENM from nanoproducts

Recently some experimental data has been published on the unintended release of ENM from nanoproducts during use or disposal from ENM (e.g. Hsu and Chein 2007, Benn and Westerhoff 2008, Blaser et al. 2008, Guiot et al. 2009, Nguyen et al. 2009, Vorbau et al. 2009). Such data is crucial for exposure assessment.

1.3 Life cycle concepts in the framework of prospective technology assessment

Considering the fact that the life cycles for ENM are determined by their final application within nano-products, one realizes that the exposure scenarios and potential adverse effects, as well as opportunities for novel applications, are strongly dependent on the life cycle of nano-products. As indicated above (please see 1.1.), the life cycle and the design of nano-products containing ENM predetermine many factors influencing the assessment of ENM exposure. Life cycle concepts of nano-products reveal information on the following issues (Som et al. 2009, Som et al. submitted):

- what kinds of ENM (chemical , functionalization, size distribution, morphology etc.) are used in what amounts in what kind of marketed or future products (prospective technology assessment (Von Gleich et al. 2008))
- the mode of ENM integration in nanoproducts
- the anticipated quantitative diffusion of nano-products on the market (prospective technology assessment)
- during what life stages of nano-products may ENM get released, triggered by what external factors such as abrasion, UV, water, detergents, sweat, etc.
- in what technosphere (waste water treatment, recycling system, waste incineration, landfill) or environmental compartmens (air, water, soil) is the release of ENM probable (exposure routes, potential uptake paths),
- in what form may the ENM get released e.g. as free ENM, in an agglomerated or aggregated form, ENM embedded in nano- or micro-sized particles, pristine or transformed, or functionalized ENM (Koehler & Som 2009).

Life cycle concepts allow one to systematically collect qualitative and – if available - quantitative data on these issues by exploiting the scientific literature as well as expert interviews in order to find implicit knowledge and experiences on the use and unintended release of ENM. Thus, life cycle concepts support priority setting for ecotoxicology and toxicology.

The term “Life Cycle Concepts” refers to methods that focus on the life cycle of products, such as Life Cycle Assessment (LCA, ISO 14040 series), design for environment, life cycle management, life cycle costing, material flow analysis, product road-mapping, value chain analysis, and many other (Davis 2007). Depending on the aim of the study, an appropriate life cycle method and scope have to be chosen. Most of the methods consider all stages of a nano-product’s life cycle (production of ENM,

transport to a manufacturer, manufacture of the ENM-containing product, use of the product(s) and recycling or final disposal of the product(s)), or focus on specific parts of the life cycle.

The strongly formalized method of Life Cycle Assessment (LCA) takes into account all inputs (i.e. materials, energy, chemicals, land use etc) and all outputs (i.e. emissions, solid waste, products etc) throughout the life-cycle of a product. LCA thus evaluates the overall impacts of a product system on the natural environment, human health, natural resources, and the man-made environment (Udo de Haes and Lindeijer 2002). Thus, LCA is essentially a comprehensive tool for the environmental sustainability assessment of nano-products, while identifying what opportunities are available for upstream or downstream improvements (e.g. emission and energy consumption reductions) (Sweet and Strohm 2006). Consequently, LCA may support the exploitation of the sustainability potential of nanotechnologies. But there is an urgent need for actual data for the nanotechnological production methods; furthermore the specific potential risks of ENM have not been included in the LCA studies so far due to a lack of knowledge relating to the effects of ENM on human health and the environment.

Other life cycle methods that are less formalized and more qualitative in nature than LCA are more directed towards the specific risks of ENM and may provide detailed information relevant to exposure scenarios as described at the beginning of this chapter. From this information, advice may also be deduced also for the safe handling of ENM and nano-products and for the safe design of nano-products (i.e. increased immobilisation of ENM in nanoproducts throughout the product life cycle).

Furthermore, life cycle concepts in general may also indicate other ENM specific risks such as for example: hazardous waste generation, the use of ancillary chemicals, hazardous by-products, the consumption of scarce materials, the dissipation of materials, cross product contamination by ENM and changed product recyclability of the ENM-containing nanoproducts.

The integrated and comprehensive approach of life cycle concepts as part of prospective technology assessment may mitigate the deficiencies in the data base of risk assessment, as mentioned in SCENIHR (2009, Sweet and Strohm 2006) by:

- setting priorities for (eco)toxicology and environmental studies
- providing a holistic view of the risks caused by the use of ENM
- providing a prospective view on risks caused by the use of ENM and thus mitigating the lagging of risk assessment and regulation behind the technological development
- providing a holistic view of the opportunities and sustainability potentials of ENM
- integrating fragmented knowledge and establishing integrated and holistic overviews of nanomaterials in the context of specific applications,
- giving advice for the safe handling of ENM and safe design of nano-products

2 Identification of the main potential risks of nanomaterials in the future

Life cycle concepts provide an expanded view of risks. Apart from the risks to human health and the environment other relevant risks of using ENM may also be identified such as:

- hampering the recycling pathways for other materials,
- the consumption and dissipation of scarce material (Som & Koehler submitted),
- hazardous waste generation.

Experience with conventional chemicals has shown that even chemicals considered to be contained in a product without any direct environmental exposure and in products that are considered to be recycled completely (e.g. computers, furniture), may get released to the environment in significant amounts, and often in pathways not considered relevant before (Mielke and Reagan 1998, Webster et al. 2009). It is also becoming increasingly evident that some chemicals contained in polymers and composites may end up in the environment and that many products containing plastics release small amounts of particulates into the surroundings. It is thus not necessarily the case that ENM contained in composites pose no environmental release threat during use. These aspects need to be considered in future assessment of certain nano-products categories.

The investigation of the potential bioaccumulation of ENM needs to be studied in much greater detail, although initial results do not indicate any great potential of ENM to be bioaccumulated. However, studies need to be performed with ENM actually released under realistic conditions.

Modelling based on the life-cycles of different product categories has shown that the type of product category in which the ENM is used is one of the most important parameters that determines which environmental compartment will be exposed. If in the future significant changes in the use of nano-products occurs or if new uses come up, then completely new exposure scenarios may become important and dominate.

4 According to our experiences industry and researchers need information on the following:

- What are the real opportunities and the risks of specific ENM throughout the nano-product life cycle?
- What alternative substances to ENM may be used for the same opportunities (alternative assessment)?
- What factors have to be considered when designing safe nano-products of high quality?
- What is the effectiveness of the possible measures to be taken in order to make the production and use of ENM safe? Here, an evaluation is extremely needed.

3 Identification of the issues to be discussed at the hearing

The hearing could clarify the needs of industry and researchers in order to accomplish a safe, integrated and responsible innovation and reveal ways for these needs to be addressed? 4

Certainly, there is an urgent need for a practical approach to implementing tools for self-control or guidelines on how to use existing assessment approaches. This practical approach has to be flexible in order to deal with the “moving target”. In the following chapters we will identify in detail which open issues should be put on the agenda of the hearing from our point of view as a part of this general theme.

3.1. Issues for discussion in the framework of the Precautionary Matrix for Synthetic Nanomaterials

For a further development of this tool as well as a possible integration into other ongoing activities in Europe, it would be advantageous to hold a general discussion of

- the practicability and applicability of the Precautionary Matrix, and
- ways that possible weaknesses in it could be mitigated

On a more scientific basis some of the principal concepts applied in the Precautionary Matrix should receive further attention:

- Can larger agglomerates of primary nanoparticles deagglomerate under physiological or environmental conditions?
- The inclusion of ENM in a range up to 500 nm into the nanospecific discussion
- The concept of nanoparticles and nanorods as primary source of potential risks to health and the environment

All relevant documents regarding the Precautionary Matrix in the English language are accessible at:
http://www.bag.admin.ch/themen/chemikalien/00228/00510/05626/index.html?lang=en.

3.2 Exposure assessment

In order to determine the environmental exposure to ENM their sources have to be known. To date very little is known about this. The following points should receive attention:

- get reliable data on the total production and usage of ENM
- get reliable data on the forms of ENM in products
- get information on the release of ENM from products during production, use and disposal

This data is needed to feed into current exposure modeling approaches and is as important as the data on the environmental fate and effects of ENM.

3.3 Life cycle concepts in the framework of prospective technology assessment

In order to mitigate the knowledge gaps in risk assessment and the rapid technology development in the field of nanotechnologies, an integrated and prospective view of the risks of ENM should be part of any informed decision-making and the priority-setting for further risk assessment studies:

What forms and types of ENM have to be investigated in the field of toxicology and environmental science? A great variety of pristine and functionalized (dotation, coating, composite) ENM are used in nano-products and they may get released in different forms (e.g. free ENM, in an agglomerated or aggregated form, embedded in nano- or micro-sized particles, pristine or transformed, or functionalized).

What are other relevant risks apart from the unintended effects of ENM on human health and the environment (e.g. consumption of scarce materials and recycling or disposal problems of nano-products containing ENM)?

. How may prospective approaches be integrated in risk assessment in order to cope with the fast technology development?

Last but not least, the evolving knowledge from risk assessment and life cycle concepts would seem to be valuable for innovation in the field of nanotechnologies. Thus, this knowledge should be exploited more consciously and systematically (e.g. medical products could take advantage of the knowledge on ENM-cell interaction, the results from release experiments may improve the design (functionality, immobilization of ENM)).

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Submission: 53

Organisation Friends of the Earth Australia

Type NGO

publishing Yes

Comments Friends of the Earth Australia believes the following areas have not received adequate attention:

1. The need for precautionary management of nanomaterial risks, with sales of nano-products halted until appropriate nano-specific risk assessment can be developed, validated and mandated.

- Particular attention should be paid to a recent review (Aitken 2009) of EHS research on nanomaterials conducted worldwide has identified three nanomaterials as potentially needing a precautionary approach to risk assessment: carbon nanotubes, nanosilver and titanium dioxide. The latter two materials are used in foods or food contact materials.

2. The need to broaden the definition of nanomaterials to encompass particles up to 300nm in size to ensure that this definition is biologically relevant.

- A growing numbers of nanotoxicologists recognise that the emerging definition of nanomaterials as measuring 100nm in one dimension or less is inadequate (eg see evidence given to the Nanotechnologies and Food Inquiry held by the UK House of Lords Science and Technology Committee 2009). Leading nanotoxicologists warned the UK House of Lords that the 100nm definition excludes biologically relevant nanoparticles a few hundred nanometres in size, which present similar nanotoxicity risks.

3. The assessment of soluble nanoparticles (eg micelles, nano-liposomes, nanoemulsions and nano-encapsulated active ingredients) as nanoparticles.

- Given the poor understanding we have of how the far greater bioavailability, solubility and potency of nano-formulated soluble substances will influence their biological behaviour and potential toxicity, it is essential to subject these nanomaterials to new nanotechnology-specific safety assessments and exposure metrics.

4. The role of aggregation, agglomeration, de-aggregation and de-agglomeration of nanomaterials.

- Where toxicity is driven by surface characteristics, the toxic properties of aggregated nanoparticles may be very similar to that of the primary nanoparticles that compose them. Agglomerates have similar structures and surface properties to aggregates and so may also share the toxicity risks associated with the primary nanoparticles that compose them. Additionally, in principle agglomerates can also change shape or come apart (Maynard 2007). If particles do not de-agglomerate, their size could reduce their bioavailability relative to that of their primary nanoparticles (Limbach et al.2005). However this may not

necessarily reduce their toxicity.
- 5. The public health implications of widespread use of potent antibacterial nanomaterials such as silver. See our recent detailed report on nano.foe.org.au
- 6. The public health implications of widespread sales of nanofoods. We are especially concerned that the public health implications of nanotechnology's use in foods has not been the subject of rigorous scientific assessment.
- 7. The need for strict precaution in managing occupational exposure risks. The emerging risk of carbon nanotubes, may only be the tip of the iceberg.

Friends of the Earth Australia: response to request for public consultation

1. The need for precautionary management of nanomaterial risks, with sales of nano-products halted until appropriate nano-specific risk assessment can be developed, validated and mandated

A recent review (Aitken 2009) of EHS research on nanomaterials conducted worldwide has identified three nanomaterials as potentially needing a precautionary approach to risk assessment: carbon nanotubes, nanosilver and titanium dioxide.

The latter two materials are used in foods or food contact materials.

A closer inspection of the scientific research to date clearly requires a precautionary approach to managing nanomaterial risks. The scientific justification for requiring proponents to demonstrate the safety of nano-products before they can be sold was accepted in 2004 by the United Kingdom's Royal Society and Royal Academy of Engineering. In their seminal report they recommended that: nanomaterials be treated as new chemicals; nano-ingredients in products be required to pass rigorous safety assessment before commercial use is permitted; nano-ingredients in products be labelled; nanomaterials in factories and workplaces be treated as if they were hazardous; and the environmental release of nanomaterials be avoided as far as possible (UK RS & RAE 2004). Global reinsurance agent Swiss Re called even more explicitly for precautionary management of nanotechnology risks: "In view of the dangers to society that could arise out of the establishment of nanotechnology, and given the uncertainty currently prevailing in scientific circles, the precautionary principle should be applied whatever the difficulties" (Swiss Re 2004, p47).

The 1992 Rio Declaration on Environment and Development describes the precautionary principle as follows: "Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost effective measures to prevent environmental degradation" (United Nations 1992). There is preliminary evidence of serious nanomaterial health and environment risks (UK RCEP 2008; SCENIHR 2009), acknowledgement by leading researchers that the extent of uncertainty is such that even design of reliable risk assessment systems for nanomaterials is impossible (EFSA 2009; Hansen 2009; Oberdörster, Stone, and Donaldson 2007) and predictions that validated nano-specific risk assessment methodologies may take up to 15 years to develop (Maynard et al. 2006). It is for circumstances such as these that the precautionary principle was intended.

Early public engagement exercises show that key public concerns relate to the capacity of governments to ensure that appropriate risk assessment takes place (Macoubrie 2006; Gavelin et al. 2007; German FIRA 2006; Halliday 2007). Yet experts including the European Food Safety Authority agree that it is as yet impossible to design nano-specific risk assessment procedures in which we can have confidence (EFSA 2009; Hansen 2009; Oberdörster, Stone, and Donaldson 2007). It would be a major breach of the public's trust to permit the ongoing sale of nanoproducts including sensitive items such as foods, cosmetics and sunscreens, which contain manufactured nanomaterials that may introduce serious new risks to human health and the environment.

We note that given the huge uncertainties surrounding the physiological behaviour and toxicological risks of nanoparticles and the lack of reliable nanoparticle detection methodologies, the Austrian Health Ministry has called for a European-wide moratorium on nanofoods until validated methods for identification and risk assessment have been developedi.

2. The need to broaden the definition of nanomaterials to encompass particles up to 300nm in size to ensure that this definition is biologically relevant

Friends of the Earth Australia observes that growing numbers of nanotoxicologists recognise that the emerging definition of nanomaterials as measuring 100nm in one dimension or less is inadequate (eg see evidence given to the Nanotechnologies and

Food Inquiry held by the UK House of Lords Science and Technology Committee 2009). Leading nanotoxicologists including Jonathan Powell from Elsie Widdowson Laboratory, Cambridge and Professor Ken Donaldson from Edinburgh University warned the UK House of Lords that the 100nm definition excludes biologically relevant nanoparticles a few hundred nanometres in size, which present similar nanotoxicity risks. For this reason Friends of the Earth recommends defining nanoparticles as 'particles having one or more dimensions measuring approximately 0.3 nanometres (nm) to 300 nm, or particles which have structures that exist at this scale' for the purposes of health and safety assessment. That is, we recommend that 300nm be the particle size at which nanoparticles are considered to be new chemicals and requirements for new health and safety assessments are triggered.

This definition of nanoparticles must include soluble particles, and also aggregates and agglomerates composed of nanoscale particles or which have nanostructures.

Particles that fall outside the size range deemed to encompass nanoparticles – even if they are not much bigger and also exhibit novel, nano-specific behaviour - will not be assessed as new chemicals. These particles will not trigger new health and safety assessments where substances have previously been approved for use in larger particle form. Inappropriate metrics that apply to larger particles will be used to measure exposure or commercial use quantities. This makes it particularly important not to set too narrow a size-based definition of nanoparticles.

Particles up to a few hundred nm in size share many of the novel biological behaviours of nanoparticles than <100nm in size, including very high reactivity, bioactivity and bioavailability, increased influence of particle surface effects, strong particle surface adhesion and strong ability to bind proteins (Cedervall et al. 2007;
Garnett and Kallinteri 2006; Linse et al. 2007). As with even smaller particles, particles <300nm in size have the capacity to be taken up into individual cells (Garnett and Kallinteri 2006). Particles up to a few hundred nm in size may also pose similar health and environment risks to particles <100nm.

Studies published last year which found that carbon nanotubes can cause the same disease as asbestos fibres received world wide attention (Poland et al. 2008; Takagi et al. 2008). Yet many of the nanotubes in the studies measured >100nm and so would not be considered to be 'nanomaterials' using a <100nm size-based definition.

Poland et al. (2008) found that two samples of long, tangled multi-walled carbon nanotubes caused asbestos-like pathogenicity when introduced into the stomachs of mice. One of their two samples had a diameter of 165nm and a length of greater than 10µm. Similarly, Takagi et al. (2008) found that in a long term study, more mice died from mesothelioma following exposure to multi-walled carbon nanotubes than died following exposure to crocidolite (blue) asbestos. In this study >40% of sample nanotubes had a diameter >110nm.

Several studies have also reported nanomaterial-like biological behaviour in particles 200nm in size - suggesting strongly that even 200nm is not an appropriate upper limit for defining nanoparticles. In an in vitro study Ashwood et al. (2007) found that 200nm particles of titanium dioxide adsorb bacterial fragments to their surface and 'smuggle' these into human intestinal tissue where they mimic invasive pathogens and can provoke inflammation. Linse et al. (2007) found that in an in vitro study, along with smaller nanoparticles, the large surface area and surface charge of 200nm nanoparticles catalysed protein fibrillation (misfolding). Protein fibrillation is involved in many human diseases, including Alzheimer's, Creutzfeld-Jacob disease, and Type 2 diabetes. Cedervall et al. (2007) also found strong interactions between proteins and 200nm particles.

Given the early evidence of novel, nano-specific behaviour, bioavailability and potential to cause harm, it would be scientifically indefensible to exclude particles 100-300nm from new nanotechnology-specific safety testing requirements and nanoparticle-appropriate exposure metrics.

Friends of the Earth Australia further recommends recognition of 'substances with nanomaterial properties'. These are substances that fall outside the size range used to define 'nanomaterials' but which nonetheless exhibit nano-specific behaviour – eg very high reactivity, bioactivity and bioavailability, increased influence of particle surface effects, strong particle surface adhesion and strong ability to bind proteins.

We recommend that if a material is recognised as a 'substance with nanomaterial properties' it must be assessed using safety testing procedures and metrics developed for nanomaterials. For example in an in vitro study Magrez et al. (2006) found that flake-like carbon black particles of different sizes <1,000nm reduced cell proliferation, led to cell death and were consistently more cytotoxic than carbon nanofibres or carbon nanotubes. These carbon black particles should be subject to nano-specific safety testing and

exposure and commercial use metrics, rather than being treated as the equivalent of bulk carbon. Recognising 'substances with nanomaterial properties' that fall outside the sizebased definition of nanomaterials will be especially important if the more narrow definition of nanomaterials measuring <100nm in at least one dimension is adopted.

3. The assessment of soluble nanoparticles (eg micelles, nano-liposomes, nano-emulsions and nano-encapsulated active ingredients) as nanoparticles

Friends of the Earth Australia emphasises that soluble nanomaterials (eg micelles, nano-liposomes and nano-encapsulated active ingredients) must be included within the definition of 'nanoparticles' and subject to nanotechnology-specific risk assessment and exposure metrics. We reject the proposal from some quarters to leave soluble nanoparticles subject to conventional risk assessment processes and conventional mass metrics to measure exposure.

Nano-sizing or nano-encapsulating food additives including vitamins, enzymes or preservatives results in greater bioavailability, improved solubility and increased potency of these substances compared to larger or micro-encapsulated form (Mozafari et al. 2006). These novel of these nanomaterials are already being exploited commercially. For example AquaNova markets its nanoscale micelles for use in foods and cosmetics because they deliver "significantly higher bioavailability" of enclosed active ingredients once ingested or applied to the skin (AquaNova undated). Omega 3 food additives have in the past been added to food in 140-180,000 nm micro-capsules, for example micro-encapsulated tuna fish oils used by Nu-Mega Driphorm® to fortify Australia's Tip Top bread line (Personal communication with Nu-Mega representative 2007). However to increase the Omega 3 potency, companies such as Aquanova and Zymes are now selling 30-40nm nanocapsules of Omega 3 – 4,000 times smaller than the Nu-Mega range (Halliday 2007).

If nano-nutritional additives and supplements provide an excessive dose of some vitamins or nutrients these may have a toxic effect or interfere with the absorption of other nutrients. Dr Qasim Chaudhry who leads the nanotechnology research team at the United Kingdom's Central Science Laboratory warns that nanoparticle and nanoencapsulated food ingredients "may have unanticipated effects, far greater absorption than intended or altered uptake of other nutrients, but little, if anything, is known currently" (Parry 2006).

Given the poor understanding we have of how the far greater bioavailability, solubility and potency of nano-formulated soluble substances will influence their biological behaviour and potential toxicity, it is essential to subject these nanomaterials to new nanotechnology-specific safety assessments and exposure metrics.

3. The role of aggregation, agglomeration, de-aggregation and deagglomeration of nanomaterials

If nanoparticles fuse together, they form aggregates which are hard to separate.

These nano-structured aggregates may be larger than 100nm – or even larger than 300nm. However in many instances aggregates will have close to the same surface area as the nanoparticles they are made from and will have 'nooks and crannies' on their surface structure that are nano-sized (Maynard 2007). Where toxicity is driven by surface characteristics, the toxic properties of aggregated nanoparticles may be very similar to that of the primary nanoparticles that compose them. In fact some early studies exposing animals to large nanoparticle aggregates showed effects that appeared to be associated with these primary particles, although the primary particles were more potent in many respects (see reviews in Maynard and Kuempel 2005, Oberdörster et al. 2007). In other instances, nano-structured aggregates may result in greater damage than that associated with the primary nanoparticles. In an inhalation study using mice Shvedova et al. (2005) found that aggregates of single walled carbon nanotubes were the focal point of granulomatous inflammation.

Nanoparticles that form clusters but do not adhere so strongly together are called agglomerates. Agglomerates have similar structures and surface properties to aggregates and so may also share the toxicity risks associated with the primary nanoparticles that compose them. Additionally, in principle agglomerates can also change shape or come apart (Maynard 2007). If particles do not de-agglomerate, their size could reduce their bioavailability relative to that of their primary nanoparticles (Limbach et al. 2005). However this may not necessarily reduce their toxicity. For example Muller et al. (2005) found that

2 months after intratracheal installation of multi-walled carbon nanotubes in rats, pulmonary lesions were caused by the accumulation of large carbon nanotube agglomerates in the airways.
It is still unknown to what extent aggregates and agglomerates will break down into smaller particles in our bodies, eg after inhalation. Researchers routinely use surfactants to 'debundle' single and multi-walled carbon nanotube samples for physicochemical investigation (Blackburn et al. 2006, Lisunova et al. 2006). Biological fluids, eg the lung's epithelial lining fluid which contains both surfactants and proteins, may similarly promote de-agglomeration (Maynard 2007, Oberdörster et al. 2007) or even break up of aggregates (Donaldson et al. 2006) into smaller particles or even the primary nanoparticles or fibres. For example Maynard (2002, cited Maynard 2007) found that larger agglomerates of titanium dioxide broke into smaller agglomerates with a diameter around 100nm when exposed to a synthetic lung surfactant. Vigorous agitation also leads to disaggregation of nanotube clumps and the production of particles smaller than 100nm (Maynard et al. 2004).
The poor understanding we have of disaggregation and de-agglomeration processes and the early evidence that aggregates and agglomerates may share both surface characteristics and toxic properties with the primary nanoparticles that compose them demand that we treat these particles as nanoparticles for the purposes of health and safety assessment.

4. The public health implications of widespread use of potent antibacterial nanomaterials such as silver

There has been rapid growth in the use of antibacterial nanomaterials such as silver, zinc and titanium dioxide in food packaging, food storage containers, crockery, cutlery, refrigerators, dishwashers, clothing, cosmetics, children's toys, personal care products, household cleaners, industrial disinfectants, computer keyboards, vacuum cleaners, clothes washing machines and many other products. Professor Stokes, has warned that such widespread use could promote dangerous antibacterial resistance to both nano-silver, as well as to other antibiotics (Salleh 2009). To date over twenty cases of bacterial resistance to silver have been reported in the scientific literature (Chopra 2007).This could render ineffective the use of nano-silver and other potent antibacterial nanomaterials in a medical context (for burns victims, in wound dressings etc) where they are of most use. This is particularly concerning given that silver is experiencing a revival in hospitals across Europe, partly because of the growing bacterial resistance to commonly used antibiotics (Chopra 2007). Bacterial infections already contribute to 110,000 deaths a year in Europe.
Biocidal nanomaterials could also interfere with beneficial bacteria in sewage and Wastewater treatment relies on heterotrophic micro-organisms for organic and nutrient removal, while autotrophic micro-organisms play an important role in nitrification. Choi et al. (2008) evaluated the effect of silver nanoparticles, silver ions and silver chloride colloids on heterotrophic and autotrophic growth and found that nitrifying bacteria are especially susceptible to inhibition by silver nanoparticles.
Silver ions may inhibit the enzymes used by nitrifying bacteria (Ratte 1999), block DNA transcription and interrupt bacterial respiration and energy creation (Kumar et al. 2005).
Silver nanoparticles' inhibition of autotrophic bacterial growth was almost twice that of silver ions and colloids (Choi et al. 2008). Heterotrophic bacteria in contrast were more susceptible to silver ions versus nanosilver particles and silver chloride colloids.
Choi et al. (2008) suggested that the accumulation of silver nanoparticles may have detrimental effects on the activities of micro-organisms in wastewater treatment.
Nanosilver is more toxic than silver ions to aquatic organisms.. Navarro et al. (2008) investigated the toxicity of silver nanoparticles versus silver ions to Chlamydomonas reinhardtii. Based on total silver concentration the silver ions appeared to be 18 times more toxic than the nanosilver particles, however closer inspection revealed that when compared as a function of silver concentration the silver nano particles appeared more toxic than the silver ions alone. The researchers reasoned that silver nanoparticles contributed to the overall toxicity of silver to the algae by providing a continuous source of silver ions.
Nanosilver particle toxicity appears to be independent from silver ions. Griffitt et al. (2009) found that when zebra fish were exposed to nanosilver particles rather than silver ions, the silver level in their gills increased. Gene expression proofing suggested that the silver nanoparticles interacted with the gills in a different manner than soluble silver particles and hence the observed effects were not due only to silver ions only.
Nematodes are widely found in soils and play a critical role in the soil food web. Their functions include primary production, decomposition, energy flow, and nutrient cycling. Nematode abundance also serves

as a useful indicator in natural ecosystems to the presence of soil pollutants and ecological disturbances. Several toxicity tests have indeed been developed for this purpose, but Wang et al.'s (2009) study was the first to investigate the effect of metal oxide nanoparticles on nematodes (C.elegans). They found that both nanosilver particles and bulk silver were toxic to nematode and resulted in impaired growth and reproductive ability.
Dissolved ions were not sufficient to explain the toxicity; nanoparticle dependent toxicity was observed. In the context of sustainable soil protection Hund-Rinke et al. (2008) point to the fact that:
"…the disposal of persistent substances such as silver should be excluded, since they will not be degraded, but accumulated. Changing environmental conditions may result in undesired consequences, or adverse effects may be detected when new knowledge will be available."
There are also serious concerns that nano-antibacterials will pose unacceptable toxicity risks to human health and to environmental systems in to which waste products are released. A recent study by imminent UK nanotoxicologists advised that there is sufficient evidence to suggest that silver and titanium dioxide nanomaterials may be harmful to the environment and therefore the use of the precautionary principle should be considered (Aitken 2009).

5. The public health implications of widespread sales of nanofoods
We are concerned that the public health implications of nanotechnology's use in foods has not been the subject of rigorous scientific assessment. Nanotechnology will enable manufacturers to promote nano-reconstituted, nano-fortified or nanopackaged foods as delivering superior health benefits, hygiene or convenience than minimally processed 'fresh foods'. If this proves true, it is likely that nanotechnology will encourage even greater consumption of highly processed foods at the expense of fruits and vegetables. Beyond the need to ensure the safety of nanofood additives, it is also useful to question whether or not fortifying food with nano nutrients, or using nanotechnology to reduce the fat or sugar content of junk foods, is actually desirable from a public health perspective. For every person in the UK who suffers illness as a result of food poisoning, there are already 50 who suffer ill health as a result of poor diets and inadequate consumption of fruit and vegetables (Lang and Rayner 2001). If processed, nano-packaged food is marketed successfully as safer than eating fresh, unpackaged foods, and consumption of fresh foods declines further, it is possible that the result will actually be poorer public health outcomes.
We are also concerned that nano-fortified foods may be promoted as a substitute for a balanced diet. There is a growing number of manufacturers prepared to claim that their nano-fortified beverages or foods will meet a large part, or even the entirety, of an individual's dietary needs. For example Toddler Health's range of fortified chocolate and vanilla milkshakes ('nutritional drinks'), which include 300nm particles of SunActive® iron, is marketed as "an all-natural balanced nutritional drink for children from 13 months to 5 years. One serving of Toddler Health helps little ones meet their daily requirements for vitamins, minerals and protein" (Toddler Health undated). Yet we question the claim that fortification of highly processed foods using nano-encapsulated or nano-scale vitamins or health supplements can deliver the same health benefits as improving peoples' diets.
We are similarly concerned that the use of nanotechnology to reduce the fat or sugar content of junk foods may simply entrench and expand poor eating habits. Even a fat-reduced chocolate bar or donut will have inferior health and nutritional habits compared to fresh fruit or a 'real' meal. We suggest that the implications for public health of nanotechnology in food must be subject to rigorous, critical assessment.

6. The need for strict precaution in managing occupational exposure risks
In 2004, scientists at the highly regarded United Kingdom's Royal Society and Royal Academy of Engineering (RS/RAE) and risk experts at the world's second largest reinsurance company Swiss Re both warned that because carbon nanotubes share many physical properties with asbestos, they may also present similar health risks.
Swiss Re put it bluntly: "…some nanotubes are similar in size and form to asbestos fibres. The supposition that the potential for harm could be similar would appear to be obvious" (Swiss Re 2004, p42).
The UK RS/RAE warned that: "Exposure to fibres in industry, in the form of asbestos, is a well-recognised cause of serious illness, including cancer. The toxic properties of such fibres are dependent upon a diameter narrow enough to allow inhalation deep into the lung, a length that prevents their removal by macrophages, resistance to dissolution in tissue fluid, and a surface able to cause oxidative damage... Carbon and other nanotubes have physical characteristics that raise the possibility of similar toxic properties... Such materials require careful toxicological assessment and should be treated with particular

caution in laboratories and industry" (UK RS/RAE 2004, p50).

In 2004 the RS/RAE recognised that serious knowledge gaps compromised our ability to predict whether carbon and other nanotubes could pose asbestos-like risks.

The RS/RAE recommended that: "Given previous experience with asbestos, we believe that nanotubes deserve special toxicological attention; the types of studies that are required are listed in Box 5.4" (UK RS/RAE 2004, p43).

Key gaps remain in our understanding of the health risks posed by carbon nanotubes and these require urgent attention. These gaps include: understanding whether airborne nanotubes will reach the lungs in realistic occupational or environmental conditions; potential for long-term inhalation/ exposure at realistic exposure levels to result in mesothelioma and/ or other serious disease; occupational exposure levels likely to be faced by workers across a range of sectors and jobs; role of size, shape and other nanotube properties in affecting the potential for acute toxicity; role of size, shape and other nanotube properties in affecting the potential for fibrosis, cancer and/ or other disease; the role of aggregation, agglomeration, and disaggregation and de-agglomeration in affecting nanotube properties and toxicity; long-term biodurability of nanotubes; and the potential for nanotubes release from products over their life-cycle.

However the majority of the critical preliminary questions the UK RS/RAE identified regarding the biological behaviour of carbon nanotubes have been answered. The published literature suggests strongly that some forms of nanotubes could pose similar health risks to asbestos and that a wide range of nanotubes cause both localised and system toxic effects. Given early evidence of the potential for a repeat of the asbestos tragedy, there is no acceptable reason for postponing measures to stop the further commercial production and sale of carbon nanotubes until further research can identify whether or not any levels of nanotube exposure can be deemed safe.

In recent years, evidence has mounted that exposure to carbon nanotubes can cause asbestos-like disease, acute toxicity, accelerated development of artery 'plaque' responsible for heart attacks, cell death and DNA damage far from the site of exposure:

- Nanotubes that look like asbestos behave like asbestos: long, multi-walled carbon nanotubes introduced into the mice abdominal cavity caused asbestos-like pathogenicity in a 7 day in vivo study (Poland et al. 2008)
- Nanotubes caused more deaths from mesothelioma than did the most potent form of asbestos following their introduction into mice abdominal cavity in a 180 day in vivo study (Takagi et al. 2008)
- In instillation in vivo studies where sufficient quantities of nanotubes reached the lungs, nanotubes caused inflammation, fibrosis and granulomas (Lam et al. 2004, Muller et al. 2005, Shvedova et al. 2005)
- Comparative in vivo study finds intratracheal instillation of multi-walled carbon nanotubes caused inflammation and severe pulmonary damage; inhalation resulted in moderate pathological lesions (Li et al. 2007)
- Reviews of the published literature on carbon nanotubes highlight large persisting knowledge gaps but indicate that SWCNTs and MWCNTs may have the potential to cause severe lung disease and possibly cancer (Donaldson et al. 2007; Lam et al. 2006; Muller et al. 2006;)
- Lung proteins preferentially bound to carbon nanotubes in an in vitro study, indicating the potential for damage to lung immune defence mechanisms, increased risk of lung infections and emphysema (Salvador-Morales et al.2007)
- Nanotubes caused the accelerated development of artery plaque responsible for causing heart attacks and strokes, and damaged DNA in the hearts of test mice in an in vivo study (Li et al. 2007)
- Carbon nanotubes were taken up by cell nuclei in an in vitro study where they caused dose-dependent cell death (Porter et al. 2007)
- Multi-walled carbon nanotubes localised within skin cells in in vitro studies, caused irritation, impaired protein function and decreased cell viability. The authors warn this could cause skin disease (Monteiro-Riviere et al. 2005; Witzmann and Monteiro-Riviere 2006)

To avoid a repeat of the asbestos tragedy, Friends of the Earth Australia is calling for an immediate moratorium on the commercial use of carbon nanotubes and the sale of products that incorporate nanotubes until research can demonstrate whether or not there is any safe level of exposure to them.

Given the evidence of vastly greater health risks of carbon nanotubes, it is completely unacceptable that permissible occupational exposure levels to carbon nanotubes and materials safety data sheets provided to workers should remain based on synthetic graphite. The absence of reliable, affordable detection technologies for routine occupational exposure measurement to carbon nanotubes is also very concerning (Tantra and Cumpson 2007).

Before any further commercial use of carbon nanotubes, we are calling for new nanotechnology-specific regulation to protect workers, the public and the environment. This must include nano-specific safety assessments for nanotubes and all other manufactured nanomaterials, requiring full physico-chemical characterisation and a comprehensive range of safety tests. Metrics used must also be appropriate to nanomaterials (ie particle surface area and number of particles rather than mass). New permissible exposure levels must clearly be enforceable.
This requires the development of cost-effective, reliable technologies for routine occupational exposure measurement.
Carbon nanotubes must be subject to safety assessment as both nanomaterials and as fibres. MWCNTs that are demonstrated to cause serious health harm may measure up to 200nm in diameter. As key mechanisms for harm associated with MWCNT and other particles in this size range appear to be oxidative stress, inflammation and protein interactions commonly associated with particles <100nm in size, we call for all particles and materials measuring up to 300nm in size to be subject to nano-specific safety assessment and metrics. Given that the other key mechanism for nanotube-related harm appears to be their behaviour as respirable, persistent high aspect ratio fibres, we also support calls for their toxicity to be assessed alongside asbestos and other fibres as part of a unified strategy.

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Submission: 54

Organisation Aquanova

Type NGO

publishing Yes

Comments

See attachment

Submission: 55

Organisation EEB and BUND ((Friends of the Earth Germany)

Type NGO

publishing Yes

Comments The issues surrounding the wide spectrum of potential risks and possible benefits associated
with the rapid advance of modern nanotechnologies are of high interest for the European Environmental Bureau and BUND from the standpoint of environmental civil society groups. These include the current realities of nanotechnological hazards, their impact vis-a-vis nanotech-risks and benefits, and the consequent repercussions on the public, society and the environment. Our central idea is that the technological risks must be properly and timely communicated to the public (along with the benefits) to ensure the democratic, responsible and safe development of this emerging technology. We also consider that beyond a public hearing on nanotechnologies and related risks, the European Commission should host a public debate on technological innovation as such in the context of sustainability (sustainable production and consumption).
Meanwhile, EEB demands that no further market introduction be allowed for products containing manufactured nanomaterials which could lead to exposure of consumers or uncontrolled release in the environment. Such a restriction should be put in place until appropriate impact and safety assessment tests are developed and appropriate nanospecific risk assessment carried out and mandated that provide scientific proof that these materials and products are adequately safe to human health and the environment. Those products already on the market should be should be removed from commercial circulation until proven safe.
1. Identification of any possible topics which have not been covered in the opinions from the relevant EU Risk Assessment Committees and Bodies
1.1 Environmental impacts of nanomaterials have not been addressed in depth
For an adequate risk assessment to be conducted it is critical to have information on the amount of engineered nanomaterials (ENMs) dispersed in the environment as well as have the understanding of their environmental impacts. The Royal Commission on Environmental Pollution states: “Difficulties also arise because the form in which materials make their way into the environment might not be the same as that encountered during manufacture. Many free nanoparticles agglomerate and aggregate in the natural environment, forming larger structures that may have different toxicological properties to those exhibited by original nanoform”1. EU Scientific Opinions barely addresses the results of relevant ecotoxicological

studies and do not discuss the broader environmental impacts of nanomaterials even when there is data on ecotoxicology available.

1.2 Lifecycle approach in risk assessment

Nanomaterial lifecycle assessments – including manufacturing, transport, product use, and end-of-life management – need to be undertaken to understand the potential hazards and assess the probability and severity of adverse effects of ENMs. This approach has also been requested by the UK Royal Society and the Royal Academy of Engineering2.

1 Royal Commission on Environmental Pollution 2008: Novel Materials in the Environment: The case of nanotechnology.

2 The Royal Society and the Royal Academy of Engineering, (2004).Nanoscience and nanotechnologies: opportunities and uncertainties, pp. 85-88.

1.3 Toxicological and exposure data for many emerging nanomaterials are missing

The lack of toxicological and exposure data for many emerging nanomaterials is a critical gap for risk assessment. Furthermore, there is little to no specific information about exposures to engineered nanomaterials although the potential for human exposure could be significant in workplaces or via consumer products. Together, these gaps contribute to uncertainty about whether or not nanomaterials are ‘‘new’’ and whether or not they pose ‘‘novel’’ and significant risks to the environment and human health, which is key information for enacting preventive statutes as well as regulations.

1.4 Assessment of actual human and environmental exposure

Little to nothing is known about actual and long term human exposures to engineered nanomaterials in real workplaces or the environment, or what levels of exposures are likely to be harmful3. If available, information on exposure comes from industry, which is not verified by independent regulatory or scientific bodies. In the EU Scientific Opinions no data can be found regarding the current and prospective exposure of humans and the environment.

1.5 Migration of ENMs

Like other substances, nanomaterials could migrate from materials in which they are supposed to be “bound”, leading to consumer and environmental exposure. EFSA stated in its opinion on “The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety” that “(…) few studies indicates that some ENM may migrate while others do not. Migration is likely dependent on the type of ENMs and FCM and no general conclusion can be drawn.” Therefore more data on nanomaterials fate in the environment is urgently necessary to determine and study the possible exposure routes and affected environmental media.

1.6 Next generation of ENMs4

EU Scientific Committees have not yet examined the safety challenges and ethical implications of next generation nanomaterials, which may range from relatively simple active nanomaterials, such as drug delivery systems already entering the market, to complex interactive nanotechologies for human enhancement and use in synthetic biology. According to the Washington based Woodrow Wilson Centre for Scholars future generations of nanomaterials are likely to have wide-ranging impacts and will hardly be manageable within the current scope of legislation5. It is therefore high time for the Commission to begin assessing the safety challenges next generation nanomaterials will pose.

1.7 Combined effects of exposure to nanomaterials

EU Scientific Committees have so far failed to consider the combined effects of exposure to a nanomatierials “cocktail”. It has also not been studied how ENMs interact with each other once they have entered the human biological system or have been released in the environment . The joint impact of various ENMs is thus to be researched before any final conclusions on risks are made.

The behaviour of agglomerates formed from ENMs have also to be assessed more comprehensively. EFSA itself states that “It can be assumed that ENM agglomerates break

up under certain conditions that occur in food, feed, the gastro intestinal tract and biological tissues."

1.8 Standard Definition of Nanomaterials still missing

It is crucial to agree and adopt a standard definition of nanomaterials which will be used in all scientific opinions and will be the basis of EU legislation of ENMs. This has not been achieved to date and is detrimental to the scientific acceptance of the Risk Assessment Committees' opinions. Environmental civil society groups have proposed an extensive definition[6] that brings clarity and coherence on key aspects of nanomaterials with focus on:

- Size being defined from 0.3nm to 300nm;
- Substances having nanomaterial-like properties to be included, even though they fall beyond the official size range;
- All nanomaterials to be included in regulation including aggregates and agglomerates, and not just those that are insoluble or bio-accumulative.

2. Identification of what are, according to current scientific knowledge, the main potential risks that could emerge from the use of nanomaterials in the future

2.1 Human toxicity

Many of the properties that make the benefits of nanomaterials can also make them more likely to react with tissues in the body and cause cellular and tissue damage. A large body of research associates existing nanomaterials in the environment, such as fine and ultrafine particulates produced incidentally via fossil fuel combustion, with adverse public health effects such as respiratory problems, cardiovascular diseases, and/or increased mortality[7,8].

A growing number of studies on engineered nanomaterials show that some of these materials can have detrimental biological effects. For example, nanoscale titanium dioxides used in sunscreens and cosmetics have been associated with pulmonary effects such as lung inflammation, pulmonary damage, and fibrosis in animal studies and related effects in vitro [9,10,11].

Many different types of carbon nanotubes, which have fibrous structures similar to that of asbestos, are used in electronics, pharmaceuticals, and a variety of other applications; some forms of carbon nanotubes have been associated with oxidative stress, cytotoxicity, inflammation, granuloma formation, and fibrogenesis in in vitro and in vivo studies[12].

Fullerenes are used in catalysts, copolymers and composites, lubricants, drugs and drug delivery systems, cosmetics, health care products, and sporting goods. Due to their antioxidant properties, they show promise as treatments for cancer, AIDS, and bacterial infections, but some studies suggest that they can cause DNA damage[13].

Quantum dots, nano-sized particles used or being developed for use in electronics, biomedical imaging, and surveillance, are typically made of cadmium or lead, well-known toxins. Toxicological and pharmaceutical studies suggest that protective coatings of quantum

3 Nowack B, Bucheli TD (2007) Occurrence, behavior and effects of nanoparticles in the environment. Environmental Pollution 150:5–22.

4 Also see: Royal Commission on Environmental Pollution 2008: Novel Materials in the Environment: The case of nanotechnology.

5 Davies: Oversight of Next Generation Nanomaterials, 2009, http://pewnanotechproject.us/news/archive/davies4/

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dots can degrade in light and oxidative conditions, releasing these metals into cells and organisms and causing toxic effects14.
There are numerous other types of nanomaterials currently in production, most of which have not been studied for toxicity.

2.2 Adverse environmental effects

Engineered nanomaterials used widely for environmental applications will eventually end up in the environment. Moreover, the increasing number of nanomaterials used in consumer products and construction materials are likely to eventually find their way into air, water, and soil through waste streams when these products are discarded and/or through wear and tear15.
A small but growing number of studies have been done to date to assess fate and transport of engineered nanomaterials. Brumfiel16 reported that fullerenes dispersed in water are poorly absorbed by soils, which may allow absorption by terrestrial invertebrates. A more recent study suggests that negatively charged aggregates of C60 fullerenes may be stable in aqueous environments17. Similarly, a recent study on multi-walled carbon nanotubes shows that they can remain stable in water for up to a month18. These studies raise concerns about potential transport of these materials downstream from their emissions.
Concerns have also been raised about potential effects on wildlife and ecosystems of nanomaterials released into the environment. Fortner19 and Brayner20 showed that when micro-organisms are exposed to varying concentrations of nanomaterials (e.g., zinc oxide, buckyballs), their growth and metabolism are inhibited. Others have shown that some nanomaterials can cause hatching delays, deformities, and acute toxicity in zebrafish and/or zebrafish embryos21, 22 and respiratory distress, organ pathologies, and other physiological effects in rainbow trout23, 24. A unique study on plants suggests that some nanomaterials may inhibit seed germination and root growth25. One of the only food-chain studies to date26 showed that nano-sized zinc oxide and fullerenes are more toxic to algae than larger particles and can be transferred to higher organisms along the food chain.

2.3 Microbial resistance to antibiotics

14 Hardman R (2005) A toxicological review of quantum dots: toxicity depends on physico-chemical and environmental factors. Environmental Health Perspectives 114(2):165–172.

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SJWP.
The usage of nano silver in higher quantities in a wide range of consumer products could cause resistance of harmful microbes to the nano substance and perhaps to silver in its macro form as well. Given that a large number of harmful bacteria has already become resistant to many antibiotics, it is essential to preserve the effectiveness of silver for use as an anti microbial substance in medical applications for future generations.

3. Identification of further issues to be discussed at the hearing

3.1 Gaps in Awareness, Communication, and Training

Low capacity of policy making staff and meager public awareness and training related to nanotechnology issues, along with potential communication gaps between producers and users of nanomaterials and the risk regulators, are likely to play critical roles in how proactively any problems with nanomaterials that might arise are handled. Communicating risk thus needs to be given a priority in the public debate on nanotechnologies to ensure an informed and active participation of various stakeholder groups.

3.2 Risk assessment tools for new technologies

Development of tools for sustainability assessment of new technologies, including risk assessment for their more systematic use in both research and product development is

urgently needed. These should also be used in policy developments on innovation and ecoinnovation, and sustainable industrial policy in the EU.

Submission: 56

Organisation Federal Ministry for the Environment, Nature Conservation (Germany)

Type Public authority

publishing Yes

Comments

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