A CONSTRUCTIVE CONTRIBUTION TO THE RESPONSIBLE DEVELOPMENT AND USE OF ENGINEERED NANOMATERIALS

Insider Report

OPTIMIZING THE BENEFITS OF NANOTECHNOLOGY WHILE MINIMIZING AND CONTROLLING THE RISKS

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Key pieces of the current European legislation appear to be inadequate when it comes to regulating nanomaterials in the short and the long term

HOW ADEQUATE IS CURRENT NANOTECHNOLOGY REGULATION?

A new PhD dissertation "<u>Regulation and Risk Assessment of</u> <u>Nanomaterials – Too Little, Too Late?</u>" by Steffen Foss Hansen from <u>DTU Environment</u> at the Technical University of Denmark finds that key pieces of the current European legislation are inadequate when it comes to regulating nanomaterials in the short and the long term. Hansen furthermore finds that the chemical risk assessment framework is inadequate to timely inform policy-makers about the health and environmental risks of nanomaterials, if not in the short term, then most definitely, in the long term. The aim of the PhD dissertation was threefold:

- Investigate whether existing regulation is adequate in the short and the long term;
- Explore the feasibility of risk assessment for the purpose of dealing with the complex emerging risks of nanomaterials and finally;
- Provide recommendations on how to govern nanotechnologies.

As the public discussion about the regulation of nanotechnology in general, and nanomaterials in particular, heats up, emerging opinions on the applicability of existing regulation differ substantially and so do views on which regulatory options best address the current lack of information about environment, health and safety risks of nanomaterials, as well as the regulatory uncertainty and concerns expressed by the politicians, members of the public and industry, and investors.

Some argue that a completely new regulatory framework is needed, whereas others go even further and argue in favor of implementing a total moratorium on nanotechnology research, development and commercialization. And then there are those who argue for a laissez-faire attitude.

Understanding the limitations of the current regulation in regard to nanomaterials is a starting point in the process

towards adapting existing laws and facilitating discussion about which kind of regulatory options is best to address these.

Hansen's dissertation presents an in-depth analysis of the key pieces of the current European legislation such as the chemical and pharmaceutical regulation, as well as the worker safety directives, and waste directives. He finds that – although nanomaterials might be covered by the general scope of many of the existing legislative frameworks – it is often unclear if current regulation is actually applicable when it comes to specific nanomaterials and their diverse applications.

According to Hansen, the main concerns with regard to the European chemical legislation, <u>REACH</u> (Registration, Evaluation and Authorization of Chemicals) are that it is unclear when a nano-equivalent of a bulk substance should be registered under REACH, and that production thresholds for when (eco)toxicological information has to be submitted, are not currently met for many nanomaterials (although they might be in the near future).

Furthermore, even though companies are urged to use already existing guidelines, both the European Commission and its <u>Scientific Committee on Emerging and Newly-Identified</u> <u>Health Risks</u> as well as others have pointed out that current test guidelines supporting REACH are based on conventional methodologies for assessing chemical risks and may not be appropriate for the assessment of risks associated with nanomaterials.

"Somewhat similar issues have been raised for pharmaceuticals where the concern is that current product standards may not be suitably designed to address various aspects relating to novel applications of nanotechnology in nanomedicine," says Hansen. "Furthermore, if the estimated environmental concentration of medical products is below 0.01

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So far, the mechanisms of nanoparticle phytotoxicity remain largely unknown and little information on the potential uptake of nanoparticles by plants and their subsequent fate within the food chain is available

EXPLORING NANOTECHNOLOGY'S IMPACT ON MAJOR FOOD CROPS

Most of the nanotoxicology research currently undertaken deals with the potential risk aspects that various nanomaterials might pose for the human body. So far, the mechanisms of nanoparticle phytotoxicity – the ability to cause injury to plants – remain largely unknown and little information on the potential uptake of nanoparticles by plants and their subsequent fate within the food chain is available. Research in this area is fairly scant, and among the few studies available, none have used major food crops or carbon nanoparticles.

The interaction between nanoparticles and plants currently is poorly understood. Unlike mammalian species, plants have thick and porous cell walls and a vascular system for water and nutrients uptake. Plants in natural environment can also conduct photosynthesis. How nanoparticle uptake and their accumulation may impact on plant structure and their biological and biochemical processes remains a question. The few studies available in this field are probably only touching the tip of the iceberg.

A team of scientists at Clemson University has undertaken an effort to shed light on the impact of nanomaterials on high plants, filling a significant knowledge gap in the current literature. They showed how nanoparticles above certain concentrations could clog the vascular systems of plants. They also showed how these nanoparticles above certain concentrations could impact on seed setting.

An interesting aspect of this work is that, besides the potential risk aspects of these findings, researchers might also utilize them to deliberately inhibit the growth of certain type of undesirable plants like weeds.

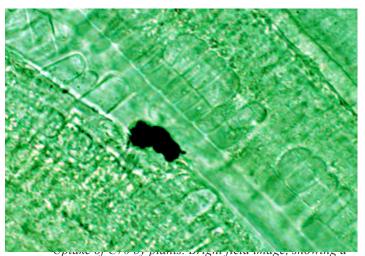
"Apart from the toxicological aspects we also wanted to illustrate the new science in this area of research by introducing some biophysical approaches to the discussion," <u>Pu Chun Ke</u> tells us. "In our recent work, we used natural organic matter (NOM), the substance abundant in the natural environment, to suspend fullerene nanoparticles. We used rice plants, the most important food crop species, as a model system. We showed the biodistribution of carbon-based nanoparticles in plants using imaging and FTIR spectroscopy, and for the first time we discovered the generational transmission of nanoparticles. All these are major advances in the field."

Ke, an associate professor who leads the Single-Molecule Biophysics and Polymer Physics Laboratory, together with professors Hong Luo and Apparao Rao, and members of their groups, have characterized the dynamic uptake, compartment distribution, and transformation of fullerene C70 in rice plants and have detected the transmission of C70 to the progeny through seeds. The team published their findings in the February 20, 2009 online edition of *Small* ("Uptake, <u>Translocation, and Transmission of Carbon Nanomaterials in Rice Plants</u>").

For their experiments, the Clemson scientists incubated newly harvested rice seeds in Petri dishes that contained 15mL of different concentrations of C70–NOM and MWNT–NOM in

rice germination buffer. After germination at $25\pm1^{\circ}$ C for 2 weeks the seedlings were transplanted to soil in big pots and grown in a green house to maturity without addition of nanoparticles.

To investigate generational transmission of nanomaterials, mature seeds from the control plants and C70treated plants were harvested 6 months after germination, and a number of seeds of similar size for each plant were chosen to again be planted in a Petri dish filled with rice germination buffer and kept again at $25\pm1^{\circ}$ C for another 2 weeks. This time, these germinated plants were allowed to grow without the addition of nanomaterials.



C70 cluster (black) formed in the vascular system (tilted channels) of a rice plant leaf. The original concentration of the C70 was 400 mg/L. (Image: Dr. Pu Chun Ke/Clemson University)

Examining the tissue of their rice plants at various development stages, the researchers frequently found black aggregates in the seeds and roots, and less frequently in stems and leaves, indicating that the sequence of nanoparticle uptake was from the plant seeds and roots to the stems and leaves.

"The appearance of black aggregates mostly in and near the stem's vascular system suggests the transport of C70 occurred simultaneously with the uptake of water and nutrients in the xylem," says Ke. "Remarkably, black aggregates were also spotted in the leaf tissues of the secondgeneration plants, though much less frequently."

According to the Clemson team, the accumulation and transformation of nanoparticles in plant tissues and cells suggests a plausible mechanism for nanoparticle uptake: a dynamic competition between nanotransport driven by water and nanoparticle convections and the physical hindrances of plant tissues and nanoparticle aggregation.

Ke explains that individual C70 nanoparticles may enter plant roots through osmotic pressure, capillary forces, pores on cell walls and intercellular plasmadesmata or via the highly

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regulated symplastic route. "Once in the plant roots and stems, individual C70 nanoparticles may share the vascular system with water and nutrients and may be transported via transpiration, the evaporation of water from the plant leaves" he says. "Individual C70 nanoparticles may also form aggregates or even clog the vascular system due to hydrophobic interaction, or may leak into nearby tissues and cells via these mechanisms."

"The integration of nanoparticles by plant species may result from the nanoparticles' small dimension and selfassembly and from the nanoparticle interactions with plant organelles and the natural organic matter," explains Ke. "The potential impacts of these processes on both food safety and the environment are important subjects to understand. Future research needs to address questions such as to what extent molecular and genetic mechanisms may mediate plant responses to nanoparticle exposure and, furthermore, how to control such responses for mitigating the adverse effects of nanomaterials on plant development."

This field of research is quickly becoming a priority area for federal funding agencies, fueled by a strong public interest in and concerns of nanotechnology. The major challenge for this area of research is its vast complexity, which can only be addressed adequately by breaking the barriers of traditional disciplines. As a testament to this statement, the Clemson team consisted of three groups in biophysics, materials synthesis, and plant biology.

A new study has found that silver nanoparticles can bind with double-stranded DNA and, possibly in this way, result in compromised DNA replication fidelity both in vitro and in vivo

NANOSILVER USED IN FOOD STORAGE MATERIALS FOUND TO INTERFERE WITH DNA REPLICATION

Silver has long been recognized for its infection-fighting properties and it has a long and intriguing history as an antibiotic in human health care. In ancient Greece and Rome, silver was used to fight infections and control spoilage. In the late 19th century, the botanist von Nägeli discovered that minute concentrations of silver contained microbiocidal properties. However, as the first antibiotics were discovered, this old household remedy was quickly forgotten.

In its modern form, silver nanoparticles have become the promising antimicrobial material in a variety of applications because they can damage bacterial cells by destroying the enzymes that transport cell nutrient and weakening the cell membrane or cell wall and cytoplasm. For instance, an increasingly popular applications is to use pure silver, or silver-coated, nanoparticles in food packaging materials such as plastic bags, containers, films or pallet.

Binding with DNA possible

A new study has found that silver nanoparticles can bind with double-stranded DNA and, possibly in this way, result in compromised DNA replication fidelity both in vitro and in vivo. But the study could not conclusively determine whether silver nanoparticles directly interact with DNA polymerases.

"Despite the wide application of nanosilver and many related studies on cytotoxicity to bacteria, there is still a serious lack of information concerning their long-term impact on human health and the environment," Zhizhou Zhang tells us. "It has been suggested that DNA loses its replication ability once the bacteria are treated with silver ions and in our recent study we quantified the replication fidelity of the rpsL gene in E. coli when nanosilver particles were present in polymerase chain reactions (PCRs) or cell cultures."

Reporting their findings in the February 2, 2009 online edition of *Nanotechnology* (Food storage material silver nanoparticles interfere with DNA replication fidelity and bind with DNA), Zhang, a professor at the Teda Bio-X Center for Systems Biotechnology at Tianjin University of Science and Technology, and his collaborators from Tianjin University and Shanghai Jiaotong University found that silver nanomaterials can directly interact with genomes.

Zhang says that, since the long-term influence of such interactions is unknown, scientists need to urgently explore this kind of interactions in detail and assess the relative safety of different nanoparticles systematically.

Silver nanoparticles can compromise DNA replication

By using a novel approach, the Chinese team provided new data in the context of silver-genome interactions that shows that silver nanoparticles induce compromised DNA replication fidelity.

They started with the fidelity of DNA amplification/replication through a polymerase chain reaction (PCR) with a nanosilver aqueous suspension.

"The PCR has been proven to be a very useful tool and a basic laboratory procedure for DNA replication in vitro" says Zhang. "The nucleotide mis-incorporation errors in PCR products can be determined by mutation assays. We used the rpsL forward mutation assay, which is a direct, time-resolved measurement for PCR fidelity. Besides, bacterial strains transformed with the wild-type rpsL gene can work as a model to detect the effects of nanomaterials on rpsL replication fidelity in vivo if the bacterial strains are incubated directly with nanomaterials."

In their study, the effect of silver nanoparticles was explored for the first time on the DNA replication fidelity in vitro and in vivo, and the direct interaction between nanosilver and DNA was observed by atomic force microscopy (AFM).

One important issue in this report is the toxicity assessment methodology of nanoparticles. Approaches for toxicity assessment of nanoparticles are not necessarily *Continued on page 5*

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ppb and 'no other environmental concerns are apparent', no further actions are to be taken for the medical product in terms of environmental risk assessment. Such pre-defined action limit could potentially be problematic since the new properties of nanotechnology-based products are expected to also affect their environmental profiles."

Hansen groups the identified regulatory gaps into two categories:

The first category deals with whether nanomaterials are covered by current legislation when it comes to 1) definitions of a substance, novel foods, hazardous waste, etc. and 2) thresholds values not tailored to the nanoscale, but based on bulk material, see e.g. REACH.

The second category relates to the lack of metrological tools and toxicological data and the fact that occupational and environmental exposure limits cannot be established with existing methodologies – as required by some pieces of legislation e.g. pharmaceuticals regulation and the safety at workplace directives.

"So far" says Hansen, "the only amendment that has been implemented is to annul the exemption status of carbon and graphite under REACH, which is deemed inadequate to address the potential risks of nanomaterials and the current regulatory uncertainty. Low use concentrations by mass in the final product as well as low production/import volumes per producers would mean that many products that entail carbon nanomaterials would still not meet the requirement to be registered under REACH."

He continues to point out another problem, which is that many pieces of European legislation require or are based on the completion of a scientific risk assessment. Ever since discussions about nanotechnology-related risks have begun, chemical risk assessment has been put forward as the number one approach (along with life-cycle assessment to some extent) in regard to understanding the risks associated with the application of one kind of nanomaterials, namely nanoparticles, in our society.

In his dissertation, Hansen evaluates the applicability of each of the four individual steps of risk assessment (i.e. hazard identification; dose-response assessment; exposure assessment; and risk characterization) in the light of the current state of knowledge and he finds that each element of risk assessment holds general as well as specific limitations and challenges.

Hansen points out that, although various levels of toxicity have been reported for numerous nanoparticles, these need further confirmation before one can say that a hazard has been identified.

Hazard identification

"Multiple studies relevant for hazard identification have been carried out on fullerenes, carbon nanotubes, quantum dots and nanoparticles, however, many of these studies are not meant to facilitate risk assessment in the sense that they use nonstandardized tests, have no coherent endpoint, and differ substantially with regard to species tested, methods of administration, dose range, way of particle preparation, duration of exposure, and effects observed and reported," says Hansen. "This definitely complicates hazard identification for most nanoparticles. Preliminary results furthermore indicate that the diversity of nanomaterials and their properties makes it an overwhelming challenge to conduct in vitro and in vivo evaluation of their biological effects. It is evident that the information provided is all over the map, making it impossible to systematically analyze the studies for properties of the nanoparticles which are important for the observed effects."

Dose-response assessment

The second element of risk assessment i.e. dose-response assessment assumes a 'no effect' threshold can be established and although some studies have reported observing a doseresponse relationship there is no evidence of a dose threshold below which nanoparticle instillation ceases to cause, for instance, inflammation.

Hansen explains that a dose-response assessment is furthermore hindered by the fact that it is unclear what the best descriptors for dose is and which properties determine or influence the inherent hazards of nanoparticles. "The current lack of characterization of the nanoparticles tested in various studies makes it impossible to identify causality between observed hazards and specific physical and chemical properties" he says. "There is furthermore substantial limitation in our ability to determine individual and multiple particle characteristics simultaneously and in a consistent manner – both prior and during tests – when using different characterization techniques and/or across laboratories."

Exposure assessment

Exposure assessment i.e. the third element of risk assessment, was found to be handicapped by difficulties in monitoring nanomaterial exposure in the workplace and the environment, and by the fact that the biological and environmental pathways of nanomaterials are still largely unexplored.

The assessment of worker exposure is made difficult by issues such as the lack of one consistent sampling method that can be used to characterize exposure in real-time and by lack of information and data, for example, about how many workers are potentially exposed, what kinds of nanomaterials workers are or might be exposed to, where and how they are exposed and at which concentrations, by dose or by particles number, and what kinds of protective measures there are used or available.

As with worker exposure, analytical methods to detect and quantify concentrations of nanoparticles in the environment have yet to become available. The total load to the environment from current of nanomaterials is unclear. Several studies have tried to assess current and future consumer and environmental exposure for individual products, nanomaterials, and applications as well as product types. Many of these have been able to apply fairly simple mathematical equations and/or information available in the European guidelines for chemical risk assessment to estimate the current and future exposure for nanomaterials.

However, in order to assess the consumer and environmental exposure to nanoparticles, numerous *Continued on next page*

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assumptions had to be made, for instance: worldwide production volumes of nanoparticles; number of products produced entailing nanoparticles and at what concentrations; current and future market penetration; release from products throughout the life-cycle of the products by mass or other relevant metric(s); to what extend products become incinerated, end up in landfills or the sewage treatment plants, or end up directly in the environment; and release from waste incinerators and removal efficacy in the sewage treatment plants, and their fate and distribution in surface water, soil and the air.

Hansen says that these studies, no doubt, hold great value in regard to assessing the applicability of exposure assessment and should be seen as 'proof of principle' rather than actual assessment of the exposure. "Paucity of knowledge and lack of access to information hampers realistic exposure assessments."

What is worrying is that the present analysis of risk assessment identified a number of limitations and flaws in relation to each of the four elements of the risk assessment framework when applied to nanomaterials. It is currently impossible to systematically link reported nanoparticle properties to the observed effects for effective hazard identification. For dose-response assessment, it was unclear whether a 'no-effect' threshold can be established and what the best hazard descriptors of nanoparticles are, and what the most relevant endpoints are.

Hansen notes that there is a serious lack of characterization of the nanoparticles tested, which makes it difficult to identify which key characteristics – or combinations of key characteristics – determine the hazards documented in (eco)toxicological studies of nanoparticles. Risk characterization being at the end of the line, the sum or maybe even the power of all of these limitations are conveyed

to estimating the risks for nanomaterials.

Considerable work is still required if future risk assessment of nanomaterials and products is to be relevant and reliable. Given that coordinated action to respond to the limitations of risk assessment and uncertainty seems to be slow in emerging, Hansen raises questions about whether risk assessment is indeed the most feasible approach to address the risk of nanomaterials.

In 2001, a report ("Late Lessons from Early Warnings: <u>The Precautionary Principle 1896 - 2000</u>") written by an expert panel commissioned by the European Environment Agency (EEA) on how to avoid repeating the mistakes of the technological development recommended looking out for 'warning signs' such as materials exhibiting novelty, persistency, readily dispersed, bio accumulative, and that lead to irreversible action.

These characteristics apply to many nanomaterials, some of which have novel properties, are capable of being incorporated in highly diverse products, may be transported to places in new ways, and may be designed to be persistent.

Hansen concludes that too little is known to predict the environmental fate of nanomaterials and feasible documentation of environmental dispersion through monitoring is not expected in the short term. "The extent to which specific nanomaterials are bio accumulative or lead to irreversible action is largely unknown, but the current state of knowledge suggests that the potential exists for such behavior under some circumstances. The global response to these warning signs has been patchy, at best. In general, government policy has been slow to respond, to gather essential data on production and to use patterns and personal protection equipment. Arguably, efforts have been better than those seen with many earlier technologies but they are still far from ideal."

NANOSILVER...

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different from those used for general chemicals, though specific approaches for nanoparticles are expected to develop, leading to the emerging field on nanotoxicology.

"Several lines of investigations have been reported to measure the safety parameters of nanomaterials, and the approaches used in those studies will be all suitable for general chemicals" says Zhang. "In our study, perturbed DNA replication fidelity resulting from nanomaterials was employed for the potential long-term toxicity assessment. This is a novel convenient method to calculate the relative capacities of different nanoparticles to introduce DNA replication errors in the rpsL gene-based assays both in vitro (PCR) and in vivo."

Another important issue in this report is the functional difference between silver nanoparticles and silver ions in the context of antibacterial activity and compromising the DNA

replication fidelity. A large number of research reports have addressed this issue already. This new paper adds to the growing body of research that provides evidence that silver nanoparticles and silver ions inhibit bacterial growth and other cellular activities under different mechanisms.

The rpsL-based assay used in Zhang's study has not been reported yet in the evaluation of the genotoxicity of chemicals, but it can be expected to play useful roles for long-term toxicity assessment for many nanomaterials. A particular challenge for future nanotoxicology research is to generate data of sufficient quality to determine if nanomaterials can influence genes, which in turn could lead to dramatically reshaped molecular network patterns in cells. On the other hand, if it is found that specific nanoparticles exhibit affinities for specific genes, then this could be used in bionanotechnology to deliberately modify genomic DNA. EFSA has concluded that established international approaches to risk assessment can be applied to engineered nanomaterials

EUROPEAN FOOD SAFETY AUTHORITY PUBLISHES OPINION ON NANOTECHNOLOGY RISKS

The European Food Safety Authority (EFSA) has published its scientific opinion on nanoscience and nanotechnologies in relation to food and feed safety. The document "The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety" is <u>available for download</u>.

EFSA's <u>Scientific Committee</u> (SC) has concluded that established international approaches to risk assessment can also be applied to engineered nanomaterials (ENM). The SC also concluded that a case-by-case approach would be necessary and that, in practice, current data limitations and a lack of validated test methodologies could make risk assessment of specific nanoproducts very difficult and subject to a high degree of uncertainty.

This opinion focuses on the use of nanotechnologies, particularly ENMs, in the food and feed chain. It elaborates on approaches and methodologies available for risk assessment of these very small particles but does not address any specific applications of particular ENMs. The European Commission (EC) asked for this opinion because consideration needs to be given as to whether existing risk assessment approaches can be appropriately applied to this new technology.

The EFSA SC recommends that additional research and investigation is needed to address the many current uncertainties and data limitations. Specific recommendations include the following:

- Investigating the interaction and stability of ENMs in food and feed, in the gastro-intestinal tract and in biological tissues
- Developing and validating routine methods to detect, characterize and quantify ENMs in food contact materials, food and feed
- Developing, improving and validating test methodologies to assess toxicity of ENMs (including reliability and relevance of test methods)

Prof Vittorio Silano, chair of EFSA's Scientific Committee, said: "The Scientific Committee has concluded that in principle it is possible to undertake risk assessments in this emerging scientific area by making use of available international approaches. However, given current data gaps and limitations in a number of cases, it may be very difficult to provide fully satisfactory conclusions.

EFSA's SC has undertaken this work as it has a multidisciplinary character and is relevant to a number of the EFSA Panels' respective areas of expertise. The SC has been assisted by a working group of scientists with relevant expertise. Feedback from a public consultation held during 2008 was taken into account before the final opinion was adopted.

EFSA's opinion will help the EC to explore appropriate measures, assess existing legislation and determine the scope of possible further requests for scientific opinions from EFSA in this field. EFSA has already received a small number of such requests and is adopting the case-by-case approach.

UPCOMING EVENTS LOOKING AT THE RISKY SIDE OF NANO

2nd European Conference for Clinical Nanomedicine April 27-29, 2009, Basel (Switzerland)

Among other topics, the conference will also address questions of sustainability, toxicity, ethics, societal and environmental impact.

Joint FAO/WHO Expert Meeting on the Application of Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications

June 1-5, 2009, Rome (Italy)

Scope: The application of nanotechnologies in all aspects of the primary production of foods of plant and animal origin; in food processing, packaging and distribution; and the use of nano-diagnostic tools for detection and monitoring in food and agriculture production.

International Conference on the Environmental Implications and Applications of Nanotechnology June 9-11, 2009, Amherst, MA (USA)

This event will help to better understand the environmental aspects of nanotechnology - from characterization, fate and transport, and environmental health and safety, to green nanotechnology and new nanotechnology applications for pollution control and remediation.

Society for the Study of Nanoscience and Emerging Technologies First Annual Conference

September 8-11, 2009, Seattle, WA (USA)

The event invites all discussions of anthropological, cultural, economic, ethical, historical, philosophical, political, and sociological aspects of nanosciences and emerging technologies.

NanoEurope 2009

September 28-30, Berlin (Germany)

It is important that the effects of engineered nanomaterials on people and the environment are well understood, and that any risks are managed in a comprehensive and transparent manner. The "Safety" theme at the event will address toxicological studies of nanomaterials, as well as considering risk management and regulatory issues.

Product Liability and Nanotechnology

November 19, 2009, webinar

This webinar will provide concrete recommendations from experienced private litigators concerning what companies making or working with nanomaterials should be tracking and doing as part of their efforts to prepare themselves.

IN SHORT – PAPERS, INITIATIVES & UPDATES

PAPER: Nanosized Zinc Oxide Particles Induce Neural Stem Cell Apoptosis

Given the intensive application of nanoscale zinc oxide (ZnO) materials in our life, growing concerns have arisen about its unintentional health and environmental impacts. In this study, the neurotoxicity of different sized ZnO nanoparticles in mouse neural stem cells (NSCs) was investigated. A cell viability assay indicated that ZnO nanoparticles manifested dose-dependent, but no size-dependent toxic effects on NSCs. *doi:10.1088/0957-4484/20/11/115101*

PAPER: Cytotoxicity and Genotoxicity of Silver Nanoparticles in Human Cells

Silver nanoparticles (Ag-np) are being used increasingly in wound dressings, catheters, and various household products due to their antimicrobial activity. The toxicity of starch-coated silver nanoparticles was studied using normal human lung fibroblast cells (IMR-90) and human glioblastoma cells (U251). The toxicity was evaluated using changes in cell morphology, cell viability, metabolic activity, and oxidative stress. The results from this research indicated mitochondrial dysfunction, induction of ROS by Ag-np which in turn set off DNA damage and chromosomal aberrations. *doi: 10.1021/nn800596w*

GOVERNMENT: UK Body Cautions About Carbon Nanotubes

The UK's Health and Safety Executive (HSE) has called for a precautionary approach to the use of carbon nanotubes (CNTs) in its new information sheet, released this month. The HSE says the information sheet <u>Risk management of carbon nanotubes</u> was prepared in response to emerging evidence about the toxicology of these materials. This information sheet is specifically about the manufacture and manipulation of carbon nanotubes and has been prepared in response to emerging evidence to emerging evidence about the toxicology of these materials. However, the risk management principles detailed here are equally applicable to other bio-persistent nanofibres with a similar aspect ratio.

SOCIETY: Industry, NGOs at Odds Over Nanotechnology Regulation

A new study has revealed deep divisions on how nanotechnology should be regulated, with environmental lobby groups seeking a moratorium until products are proven to be safe, and industry proposing that specific guidelines be supplement existing regulations. introduced to The comprehensive new review ("Mapping Study on Regulation and Governance of Nanotechnologies") of existing legislation on nanotechnology found variation in governance structures across the world and disagreement over whether voluntary codes of conduct will be enough to regulate nanomaterials. NGOs consider the existing regulatory situation to be inadequate and are urging a strictly precautionary approach. They want nanomaterials to be classified as new substances and subjected to "nano-specific" regulations, according to the report. Industry representatives are instead seeking the development of specific guidance and standards to support implementation of existing regulations, which are generally seen as adequate.

REPORT: Nanotechnology a major concern for European health experts

Contact with a wide range of chemicals and other hazardous substances at work is endangering the health of workers across Europe, and nanotechnology is one of the risks causing most concern to experts from 21 European countries. A report by the European Agency for Safety and Health at Work (EU-OSHA) – called Expert Forecast on Emerging Chemical Risks - identifies the main groups of substances which could pose new and increasing risks to workers, contributing to diseases which range from allergies, asthma, and infertility to cancers. Dangerous substances are not only found in the chemical industry, but also in occupations such as farming, nursing, construction and in many small and medium sized enterprises (SMEs) outside the chemical industry.

INITIATIVE: NIOSH Offers Interim Guidance for Worker Medical Screening, Hazard Surveillance Pertaining to Engineered Nanoparticles

The NIOSH recommendations in "Current Intelligence Bulletin 60: Interim Guidance for the Medical Screening and Hazard Surveillance for Workers Potentially Exposed to Engineered Nanoparticles," are available at NIOSH's website at <u>http://www.cdc.gov/niosh/docs/2009-116/</u>. The recommendations respond to ongoing interest by employers and other stakeholders in having authoritative occupational safety and health guidance in the manufacturing and industrial use of engineered nanomaterials. The recommendations also reflect NIOSH's ongoing leadership in providing such interim scientific guidance as research progresses for determining whether engineered nanomaterials pose risks for adverse occupational health effects.

PAPER: Quantum Dot Weathering Results in Microbial Toxicity

This is the first report of QD weathering and release of toxic core components following the degradation of surface coatings after exposure to moderate acidic and alkaline conditions. Overall, this research suggests that QDs may be safely used in a variety of applications at *circum* neutral pH. However, the release of toxic inorganic constituents during their weathering under acidic or alkaline conditions in the human body or the environment may cause unintended harm that might be difficult to predict with short-term toxicity tests. *doi: 10.1021/es8023385*

PAPER: The Impact of Toxicity Testing Costs on Nanomaterial Regulation

Information about the toxicity of nanoparticles is important in determining how nanoparticles will be regulated. In the U.S., the burden of collecting this information and conducting risk assessment is placed on regulatory agencies without the budgetary means to carry out this mandate. This paper analyzes the impact of testing costs on society's ability to gather information about nanoparticle toxicity and whether such costs can reasonably be borne by an emerging industry. It shows for the U.S that, depending on approach, costs for testing existing nanoparticles ranges from \$249 million to \$1.18 billion. *doi: 10.1021/es802388s*

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