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

nanoRISK

OPTIMIZING THE BENEFITS OF NANOTECHNOLOGY WHILE MINIMIZING AND CONTROLLING THE RISKS

Insider Report

Researchers at Ecole Polytechnique Fédérale de Lausanne in Switzerland have taken the initiative and presented a practical, user-friendly procedure for a university-wide safety and health management of nanomaterials, developed as a multi-stakeholder effort.

A PRACTICAL APPROACH TO MANAGING NANOMATERIAL SAFETY IN THE LAB

In a previous *nanoRISK* issue from last year ("Questionable safety practices in nanotechnology labs around the world", nanoRISK, 2010, vol.5, iss. 2) we showed that the nanotechnology research community does not exactly appear to be at the forefront when it comes to following, not to mention setting, standards for safe practices for handling nanomaterials. One of the most surprising results was that nearly three quarters of respondents reported not having internal rules to follow regarding the handling nanomaterials – approximately half of them didn't have rules and over a quarter were not aware of any internal regulations.

Researchers at EPFL (Ecole Polytechnique Fédérale de Lausanne) in Switzerland have now taken the initiative and presented a practical, user-friendly procedure for a university-wide safety and health management of nanomaterials, developed as a multi-stakeholder effort (government, accident insurance, researchers and experts for occupational safety and health).

"There was a need for the larger nanotechnology community synthesizing, applying or characterizing nanomaterials to have a methodology to evaluate the risk and to apply adequate protection measures to limit human exposure," says Arnaud Magrez, who leads the NN Research Group (Laboratoire de Physique de la Matière Complexe) at EPFL. "As one of the largest research institutes and one of the leaders in nanoscale science worldwide, we were committed to establish such a methodology.

Thierry Meyer, head of Occupational Safety and Health Service and his colleague Amela Groso, say that at EPFL, over 30 research groups (in basic sciences, engineering or life sciences) produce, modify or use engineered nanomaterials in approximately 100 laboratories with over 300 different associated production or characterization processes.

They point out that present knowledge on nanomaterial toxicity is insufficient for completing precise risk assessment. "Threshold Limit Values for nanomaterials do not exist nor is there standard equipment for sufficiently detailed routine exposure measurements. However, since preliminary scientific evaluations show that there are reasonable grounds for concern that activity with nanomaterials might have damaging effects on human health; the precautionary principle must be applied."

"Classical risk assessment methods – Hazard and Operability Studies (HAZOP) often used to analyze risks in chemical processes, or Failure Mode and Effects Analysis (FMEA) often used in industry to evaluate the effects of potential failure modes, etc. – would require around 2000 man/day workload; these are huge resources, nearly impossible to obtain" he says. "Some other institutions have already developed best practices guides and safety management procedures for nanomaterials. However, they mainly propose a risk analysis approach for each individual process and particle type, which is not very practical for large research centers with many different, constantly changing forms of nano-related studies and laboratories."

To develop their methodology, EPFL appointed a "Nanosafe team" consisting of three safety and health

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In spite of the earlier reports that nanodiamonds are biocompatible at the cellular level, researchers have now demonstrated that nanodiamonds can activate DNA repair proteins in embryonic stem cells, suggesting possible DNA damages.

Biomedical Applications Of Nanodiamonds Might Require More Caution

Owing to their large surface area, strong infrared (NIR) photoluminescence and magnetic properties, nanodiamonds are promising for various biomedical applications, including as drug/gene carriers and alternatives to the current bio-imaging platforms. However, the biomedical applications will hardly be realized unless the potential hazards of nanodiamonds to humans and other biological systems are ascertained.

Previous research indicated that nanodiamonds indeed are very biocompatible, certainly more so than other carbon nanomaterials. These studies showed that nanodiamonds did not produce significant amount of reactive oxygen species (ROS) and did not affect the mitochondrial function and ATP production of these cells.

The biocompatibility of nanodiamonds at the cellular level has been confirmed by many independent studies. Following these earlier cytotoxicity studies, many groups have used nanodiamonds and their functionalized derivatives for drug/gene deliveries.

Biocompatibility of Nanodiamonds at Question

In spite of the earlier reports that nanodiamonds are biocompatible at the cellular level, researchers have now demonstrated in a new study ("DNA Damage in Embryonic Stem Cells Caused by Nanodiamonds") that nanodiamonds can activate DNA repair proteins in embryonic stem cells, suggesting possible DNA damages.

"Although the observed DNA damage for nanodiamonds is much less severe than other carbon nanomaterials – e.g., multiwalled carbon nanotubes (MWCNTs) – our new findings do suggest some cautions need to be taken in future biomedical applications of nanodiamonds," says Liming Dai, Kent Hale Smith Professor in the Department of Chemical Engineering at Case Western Reserve University.

Following their first study on the cytotoxicity of nanodiamonds ("Are Diamond Nanoparticles Cytotoxic?"), this is the first genotoxicity study of nanodiamonds.

"We have already demonstrated that DNA damage is possible even for those materials, like multiwalled carbon nanotubes, that have been previously demonstrated to have limited or no toxicity at the cellular level" says Dai. "As far as we are aware, this is the first genotoxicity study on carbon nanomaterials. Our earlier work on genotoxicity of MWCNTs, together with the well-established methodologies developed in our previous study for characterizing DNA damages of embryonic stem cells, prompted us to study the genotoxicity of nanodiamonds in mouse embryonic stem cells."

Dai explains that embryonic stem cells are a unique cell population with the ability to undergo both self-renewal and differentiation with the potential to give rise to all cell lineages and an entire organism. "It has been shown that embryonic stem cells are highly sensitive to DNA damages, possibly caused by UV irradiation or exposure to nanoparticles. The sensitivity of embryonic stem cells to DNA damage prompted us to study the genotoxicity of nanodiamonds in mouse embryonic stem cells, while the well-established methodologies reported in our previous paper for characterizing DNA damages of embryonic stem cells made the embryonic stem cell as the cell of choice."

DNA Repair Proteins Get Activated

The team's results showed that nanodiamonds caused increased expression of DNA repair proteins in mouse embryonic stem cells, indicating the occurrence of DNA damage.

"We found that the pristine as well as oxidized nanodiamonds caused a slight and transient increase in p53 expression within 2-4 hours of cell incubation" says Dai. "However, no significant change in downstream biomarkers has been found in embryonic stem cells treated with the nanodiamonds, suggesting that the damage is minor and might have been repaired very quickly."

Additional experiments on apoptosis and embryonic stem cell differentiation showed that the pristine nanodiamonds were quite benign to embryonic stem cells and did not cause increased differentiation or noticeable apoptosis. However, embryonic stem cells treated with the oxidized nanodiamonds showed signs of differentiation, as well as apoptosis.

"Our genotoxicity results from nanodiamonds and MWCNTs suggest that careful scrutiny of the genotoxicity of nanomaterials is needed even for those materials that have been previously demonstrated to have limited or no toxicity at the cellular level" cautions Dai. "In our present study, oxidized nanodiamonds were demonstrated to cause more DNA damage than the pristine/raw nanodiamonds, showing surface chemistry specific genotoxicity."

He notes that – knowing that the genotoxicity of nanomaterials is surface chemistry specific – there will be considerable room for controlling/minimizing the genotoxicity by functionalization of nanomaterials.

"For this purpose, the most challenging problem that needs to be addressed is to elucidate the genotoxicity mechanism" Dai describes the required next steps in this research. "Our results from both the nanodiamonds and MWCNT studies point to ROS induced DNA damages. However, the detailed mechanisms governing the ROS generation and diffusion into the cell nuclei to cause the DNA damage are still largely unknown."

MANAGING NANOMATERIAL SAFETY…

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specialists, one nano-health and occupational hygiene expert, one insurance representative, three EPFL scientists and nanoparticles' users (production and use) and one representative of State Secretariat for Economic Affairs, to develop a procedure for managing the occupational safety and health risks relevant to research laboratories producing and using nanomaterials.

Government, accident insurance, researchers and experts for occupational safety and health were invited to meet with the Nanosafe team. These meetings eventually lead a procedure for managing the occupational safety and health risks.

The results have been published in a recent edition of *Particle and Fibre Toxicology* ("Management of nanomaterials safety in research environment").

"Our procedure consists of two parts" explains Alke Fink, who leads the Advanced Particles group at the University of Fribourg. "Using a decision tree, we sort the 'nano-laboratories' into three hazard classes (Nano 3 = highest hazard to Nano 1 = lowest hazard), which corresponds to analogue approaches applied to other hazard types (biohazard, radioprotection or chemistry). We then provide a list of required prevention/protection measures (safety barriers) for each hazard level."

The authors note that the target users of this safety and health methodology are at first researchers and safety officers. They can rapidly access the hazard class of their activity and the corresponding adequate safety and health measures. More detailed analysis of specific activities can be undertaken by safety and health experts when needed.

"According to our opinion and experience, the proposed management of nanomaterial safety is not stifling or harming innovation, as it is sometimes feared among researchers," says Magrez. "Besides the fact that it is the first user-friendly methodology, the advantage of the procedure is due to the very simple and inexpensive tools can be used to conduct the evaluation of the nano-labs. Therefore, it could be easily applied by other research institutes. It is being used at EPFL but we heard that some laboratories at the University of Fribourg are already working according to these regulations."

The EPFL team says that their paper provides a good starting point for a practical approach to nano-safety and they are convinced that it will generate further discussions.

"We hope to receive some feedback from institutions which are using and/or have modified the methodology," says Meyer. "That would make our evaluation of the methodology's performance more exact and will give us valuable support for improving it."

EUROPEAN REPOSITORY OF REFERENCE NANOMATERIALS WILL IMPROVE SAFETY ASSESSMENT

The European Commission's Joint Research Centre (JRC) has just launched the first European repository of nanomaterials with a representative range of 25 different types of reference nanomaterials.

This will support safety assessment to ensure consumer protection and confidence in many innovative applications and products. Nanotechnology is one of today's most promising technological developments.

By enabling a harmonized risk assessment the repository can contribute to the success of nanotechnology and its products. Standardized methodologies and materials are necessary to obtain worldwide comparable test results and to provide reliable data for policy and regulatory decision making.

Launching the repository, Elke Anklam, Director of the JRC Institute for Health and Consumer Protection (IHCP), said: "This unique repository fosters standardization in safety assessment and facilitates innovation by creating a common and consistent measurement framework for all stakeholders. This will both support international harmonization bodies for standardizing risk assessment as well as EU policy makers for regulatory issues."

Nanomaterials may offer a range of benefits over traditional materials and enable the development of innovative applications and products. For European industry to capitalize in the best sense from nanotechnologies, it is essential that the EU has a well-considered regulatory framework covering issues related to safe practices in the manufacturing process, consumer health, and protection of the environment. Such a framework depends on harmonized and science based risk assessment. In order to ensure the comparability of the underlying data obtained in the many international test laboratories, the availability of representative reference nanomaterials is essential.

This first European repository of nanomaterials has been created by the JRC in response to needs for safety-assessment testing from experts in the major international standardization bodies. The repository contains most types of nanomaterials currently assumed to be used in significant volumes in consumer products. Some 8000 test samples have already been distributed to European national authorities, EU-funded research projects, and have also been used in international scientific co-operation initiatives (such as the OECD Working Party on Manufactured Nanomaterials).

The nanomaterials contained in the repository are produced in collaboration with the German Fraunhofer Institute for Molecular Biology and Applied Ecology (IME) under Good Laboratory Practice (GLP) conditions. The 25 types of material include carbon nanotubes, silver nanoparticles, titanium dioxide, cerium oxide, zinc oxide, bentonite, gold and silicon dioxide.

Researchers at Iowa State University present a biophysical perspective that describes the fate of nanoparticles in both the aqueous phase and in living systems.

A Biophysical Perspective Of Understanding Nanoparticles At Large

At the core of research efforts to determine the impact of synthetic nanoparticles on the environment and living systems is a fundamental understanding of the interactions between man-made nanoparticles and natural living systems that have evolved over millions of years. Environmental toxicologists, chemists and social scientists have argued that rapidly growing production of nanomaterials will inevitably lead to an increase of engineered nanoparticles in the environment via air, water and soil.

To describe nanoparticles at large, Pu-Chun Ke, Associate Professor of Physics at Clemson University, says that it may be beneficial to acknowledge that 1) biological systems are part of the food chain and therefore an essential component of the ecosystems (i.e., the behavior of nanoparticles in biological systems and that in the environment are intertwined and often correlated); and 2) collaborations are essential for such interdisciplinary research.

"To describe nanoparticles at large, we need to take a truly interdisciplinary approach, specifically,

- the knowledge of material science, chemical engineering, and condensed and soft-condensed matter facilitates our understanding of the synthesis and physical properties of engineered nanoparticles;
- the knowledge of organic and biochemistry enables our description of the composition, reaction, kinetics, and functionalization of engineered nanoparticles in ambient, aqueous solution, and living systems;
- the knowledge of biophysics and physical chemistry underlines the energetics, assembly, and interaction between nanoparticles and solvent molecules, biomolecules, organelles, cells, and organisms, which are complementary to the information offered by molecular cell biology, microbiology, plant science, toxicology, immunology, physiology, and genetics."

Ke adds that fields such as soil science, horticulture, as well as environmental science and engineering, are just some of the disciplines that are relevant for examining nanoparticles at large.

In an article in *Physical Chemistry Chemical Physics* ("A biophysical perspective of understanding nanoparticles at large"), Ke and his coauthor Monica H. Lamm, an Associate Professor at Iowa State University, present a biophysical perspective that describes the fate of nanoparticles in both the aqueous phase and in living systems.

Rather than yet another review of the field, this article attempts to provide a reflection as well as a perspective on the biophysical inner workings, which may impact and govern the behaviors of nanoparticles at large.

"Since 2003, my lab and my collaborators have engaged in using biophysical techniques – spectrophotometry, fluorescence microscopy and spectroscopy, electron microscopy, and molecular dynamics simulations – to investigate the complex phenomena associated with nanoparticles in the aqueous phase and in living systems," says Ke. "The goal of such research was to understand the implications of engineered nanoparticles in biological and ecosystems at the molecular, cellular, and whole organism levels, in order to enable the safe and full applications of nanotechnologies."

Ke says that the integration of biophysics – using the methods of physical science to study biological systems – into the investigation of nanoparticles at large is natural considering that the advancement of nanotechnology has historically been associated with the physical properties of nanomaterials, and that biophysics is an interdisciplinary science addressing biological problems with a physical thinking.

The major purposes of the new article were threefold:

- to present the biological systems as an integral portion of the ecosystems;
- to illustrate how effectively such a marriage of biophysics, nanoscience and environmental science works; and
- to project the important scientific questions in this field, which may be addressed using biophysics and physical chemistry.

To do that, Ke and Lamm present the biophysics in describing an array of nanoparticles, namely, fullerenes and their derivatives, carbon nanotubes, quantum dots, dendrimers, and plastic in the aqueous phase and their interactions with biological and ecosystems. Specifically, they show the remarkable capacity of natural organic matter in modifying the surface properties of fullerenes and affording these hydrophobic nanoparticles water solubility, mobility, and bioavailability.

"Since the fate of nanoparticles is essentially a convolution of the physicochemistry of the nanoparticles and the perturbed host systems, we provide a parallel study on the uptake and translocation of fullerene derivatives across plant and mammalian cells," Ke explains the thrust of the paper. "To illustrate the responses of plant systems to nanoparticle exposure we show the generational transfer of fullerene through the rice plant progeny, as well as the effects of quantum dots and plastic adsorption on algal photosynthesis."

In the conclusion section of their article, Ke and Lamm highlight a number of questions regarding the interactions between nanoparticles and their host systems.

"Some of these questions may take time to address due to the limitations imposed by instrument resolution or computational cost" says Ke. "We anticipate the emergence of bionanophysics and increased contributions by researchers in the fields of experimental and theoretical biophysics, polymer science, and computer simulations."

How To Control Size of Nanoparticle Clusters For EHS Studies

The same properties that make engineered nanoparticles attractive for numerous applications—small as a virus, biologically and environmentally stabile, and water-soluble—also cause concern about their long-term impacts on environmental health and safety (EHS). One particular characteristic, the tendency for nanoparticles to clump together in solution, is of great interest because the size of these clusters may be key to whether or not they are toxic to human cells.

Researchers at the National Institute of Standards and Technology (NIST) have demonstrated for the first time a method for producing nanoparticle clusters in a variety of controlled sizes that are stable over time so that their effects on cells can be studied properly ("Stable nanoparticle aggregates/agglomerates of different sizes and the effect of their size on hemolytic cytotoxicity").

In their tests, the NIST team made samples of gold, silver, cerium oxide and positively-charged polystyrene nanoparticles and suspended them separately in cell culture medium, allowing clumping to occur in each. They stopped the clumping by adding a protein, bovine serum albumin (BSA), to the mixtures. The longer the nanoparticles were allowed to clump together, the larger the size of the resulting cluster. For example, a range of clustering times using 23 nanometer silver nanoparticles produced a distribution of masses between 43 and 1,400 nanometers in diameter. Similar size distributions for the other three nanoparticle types were produced using this method.

The researchers learned that using the same "freezing times"—the points at which BSA was added to halt the process—yielded consistent size distributions for all four nanoparticle types. Additionally, all of the BSA-controlled dispersions remained stable for 2-3 days, which is sufficient for many toxicity studies.

Having successfully shown that they could control the production of nanoparticle clumps of different sizes, the researchers wanted next to prove that their creations could be put to work. Different-sized silver nanoparticle clusters were mixed with horse blood in an attempt to study the impact of clumping size on red blood cell toxicity. The presence of hemoglobin, the iron-based molecule in red blood cells that carries oxygen, would tell researchers if the cells had been lysed (broken open) by silver ions released into the solution from the clusters. In turn, measuring the amount of hemoglobin in solution for each cluster size would define the level of toxicity—possibly related to the level of silver ion release—for that specific average size.

What the researchers found was that red blood cell destruction decreased as cluster size increased. They hypothesize that large nanoparticle clusters dissolve more slowly than small ones, and therefore, release fewer silver ions into solution.

In the future, the NIST team plans to further characterize the different cluster sizes achievable through their production method, and then use those clusters to study the impact on cytotoxicity of coatings (such as polymers) applied to the nanoparticles.

Study Analyzes Possibilities And Bottlenecks For Regulating Nanomaterials With Uncertain Risks

A new report – "Regulating Uncertain Risks of Nanomaterials" (pdf) – contains the results of a study into the regulation of nanomaterials. The study examines the possibilities and limitations for such regulation under existing legislation covering the environment, consumer protection and occupational health and safety, given the uncertain risks attached to the use of nanomaterials. The central research question is which powers authorities hold to regulate production, processing, use and the waste phase of nanomaterials (and products containing them) and the obligations that companies have to assure the safety of man and the environment.

The study was conducted on behalf of the Dutch Ministry of Housing, Spatial Planning and Environment in association with the Ministry of Social Affairs and Employment and the Ministry of Health, Welfare and Sport. Its purpose is to provide an insight into the powers for authorities to regulate the production and use of nanomaterials with uncertain risks so as to protect man and the environment, plus to provide an insight into the obligations of employers to take measures to protect workers. The questions addressed in the study concern the uncertain risks of nanomaterials and cover the following subjects:

- powers to require companies to disclose information (including risk information); powers to impose requirements, like licensing or general rules;
- powers to take measures to exclude products suspected of involving great risks from the market and the role of the precautionary principle in this respect;
- obligations for an employer to take the uncertain risks of nanomaterials into account in its occupational health policy;
- possibilities for including within the framework of the Working Conditions Act provisions covering work performed with nanomaterials;liability of employers for health damage caused by working with nanomaterials.

The study takes stock of and analyses the main national and EU legislation. Reference was made to legislative history, explanatory documents, national/EU case law, policy documents and literature. Talks were held with experts from organizations including the Netherlands National Institute of Public Health and the Environment.

Computational Models Predict Nanoparticle Toxicity

Researchers are developing computational models to predict the behavior of nanomaterials in biological systems. Such predictions will allow researchers to streamline and prioritise the toxicological testing of nanomaterials.

Enrico Burello and Andrew Worth, both scientists at the JRC's Institute for Health and Consumer Protection, describe this approach ("Computational nanotoxicology: Predicting toxicity of nanoparticles") in reviewing a recent paper by Jerzy Leszczynski and coworkers on the development of a Quantitative Structure–Activity Relationship (QSAR) model to predict the cytotoxicity of metal oxide nanoparticles ("Using nano-QSAR to predict the cytotoxicity of metal oxide nanoparticles").

Although QSAR methodologies are well-known and have been extensively used in the areas of drug discovery and chemical toxicology, their application to nanomaterials is still in its infancy. Burello & Worth's recent contribution in this domain is the JRC study published in July 2010, proposing a theoretical framework for predicting the oxidative stress potential of oxide nanoparticles.

Europ. Commission Releases 2nd Edition Of Compendium NanoSafety Cluster 2011

The European Commission has released the second edition of the Compendium NanoSafety Cluster 2011 (pdf).

The intention of the compendium is to bring together researchers, create synergy in their work, and establish links and communication between them mainly during the actual research phase before publication of results. Towards this purpose the authors give emphasis to communication of projects strategic aims, extensive coverage of specific work objectives and of methods used in research, strengthening human capacities and laboratories infrastructure, supporting collaboration for common goals and joint elaboration of future plans, without compromising scientific publication potential or IP Rights.

For several years now, the research community has responded by launching very valuable projects, marking significant technological progress both in the technology and in its safety management. Thirty projects are either completed or running and represent a total RTD investment of €112M, from the NMP and other programmes, under FP6 (11 projects, €30M) and FP7 (25 projects, €82M). These projects together with a significant number of projects supported by government resources in the EU member states and the FP7 associated states, and other projects addressing safety as side objective, represent the valuable efforts of the scientific and industrial research community for progress.

Synergy among these projects, collaboration for maximising impact, policy elaboration, planning of future actions, and international cooperation are the main aims of the NANOSAFETY cluster, a projects and stakeholders open forum.

Upcoming Events
Looking At The Risky Side Of Nano

Greener Nano
May 2-3, 2011, Cupertino, CA (USA)
"NanoEHS" and "green chemistry" have become staples in nearly every undertaking or conversation involving nanotechnology. Is this change in mindset helping the community make progress in designing greener materials and processes, and supporting effective policy?

Safety Issues of Nanomaterials Along Their Life Cycle
May 4-5, 2011, Barcelona (Spain)
The aim of the Symposium is to discuss the human and environmental impacts of nanomaterials along their life cycle from their production through their processing, use, and end of life (recycling and/or disposal).

EuroNanoForum
May 30 – June 1, 2011, Budapest (Hungary)
EuroNanoForum is a biannual event supported by the European Commission. One of the topical areas of this conference is "Society, taking a holistic approach to address societal benefits and risks".

Dilemmas of Choice. Responsibility in Nanotechnology Development
June 6-7, 2011, Rovigo (Italy)
The workshop is aimed at presenting and debating contributions from different disciplines on several issues concerning the relationship between nanotechnology innovation and responsibility.

Nanotech Conference & Expo 2011
June 13-16, 2011, Boston, MA (USA)
Nanotech 2011 is the world's largest annual nano-technology conference and expo. The "Energy & Environment" track deals with environment, health and safety issues as well as cleantech and greentech issues.

Nanotechnology - Occupational and Environmental Health
August 9-12, 2011, Boston, MA (USA)
This symposium will provide a high quality of professional presentations to scientists and engineers who wish to promote and communicate the interaction between technical advances and societal, occupational and environmental impacts in the field of nanotechnology research.

Governance and Ethics of Nanosciences and Nano-technologies
October 20-21, 2011, Warsaw (Poland)
The conference will have a particular focus on the EC Code of Conduct for responsible nano-sciences and nanotechnologies research, and activities of Member States concerning implementation of the Code will be presented and discussed. Stakeholders opinions will be heard as well.

IN SHORT – PAPERS, INITIATIVES & UPDATES

BOOKLET: OECD nanosafety work: The first 5 years

This booklet – Nanosafety at the OECD: The First Five Years 2006-2010 (pdf) – presents basic information about the OECD Nanosafety work for the public over the past five years since 2006. Starting with emphasizing the importance of Nanosafety issues, it covers highlights of activities, priority areas and major outcomes as well as outreach in dealing with safety issues arising from manufactured nanomaterials.

GRANTS: EPA awards $5m to support nanomaterials EHS research

EPA has awarded $5.5 million to three consortia to support innovative research on nanotechnology. EPA, in collaboration with the United Kingdom's Natural Environment Research Council, are leading this scientific research effort to better understand the potential risks to people's heath and the environment. The scientific information developed from the research can help guide EPA and other agencies in decisions about the safety of new materials and products that are made using nanotechnology. More information on the grants: http://www.epa.gov/ncer/uk_nano09/

PAPER: Nanoparticles shorten roundworms' lives

Even though nanoparticles are increasingly entering the environment, scientists still have a lot to learn about their biological effects. Now Chinese researchers have found that exposure to cerium dioxide nanoparticles shortens the lifespan of the roundworm *Caenorhabditis elegans* ("Nano-CeO_2 Exhibits Adverse Effects at Environmental Relevant Concentrations"). Zhiyong Zhang and colleagues from the Chinese Academy of Sciences' Institute of High Energy Physics exposed larvae of the widely used model organism *C. elegans* to 8.5-nanometer particles of CeO_2. Nanoparticles of CeO_2 have many high-tech uses, such as in catalytic converters and as polish for silicon wafers. They are also under consideration for use in eye drops and sunscreen. At the lowest concentration of 1 nM, the mean lifespan of the worms was 15 days. At the highest concentration of 100 nM, the worms lived 14 days. Compared to control worms' lifespan of nearly 18 days, the lifespan of worms exposed to nanoparticles decreased by 12% when averaged over all concentrations. The researchers think the shortened lifespan is related to oxidative stress.

PAPER: Genotoxicity of carbon nanofibers

The production of carbon nanofibers and nanotubes (CNF/CNT) and their composite products is increasing globally. CNF are generating great interest in industrial sectors such as energy production and electronics, where alternative materials may have limited performance or are produced at a much higher cost. However, despite the increasing industrial use of carbon nanofibers, information on their potential adverse health effects is limited. In a recent study, researchers examine the cytotoxic and genotoxic potential of carbon-based nanofibers (Pyrograf®-III) and compare this material with the effects of asbestos fibers (crocidolite) or single-walled carbon nanotubes (SWCNT). doi: 10.1002/smll.201001832

PAPER: Effects of particle size, density and shape on marginationof nanoparticles in microcirculation

In this work, researchers evaluated the effect of critical physical characteristics such as the particle shape, size and density on a nanoparticle's tendency to marginate towards the vessel walls in microcirculation using an *in vitro* model. Since nano-particles must escape the flow in order to approach the vascular bed and subsequently extravascular components for meaningful interactions, the design of nanoparticles strongly affects their margination, a key factor for their ultimate *in vivo* effectiveness. doi: 10.1088/0957-4484/22/11/115101

DOSSIER: Voluntary approaches by industry in the field of nanomaterials

The current voluntary approaches to the regulation of nanotechnology are characterized by a broad variety and major differences. At present, there are registers, codes of conducts, certification schemes and risk management systems. In addition, even within the same type noticeable differences can be observed. For instance the BASF code of conduct is restricted to enterprises while that of the IG-DHS is restricted to a certain region and to a specific sector (food). In contrast, the EU code of conduct not only applies to the whole of the EU, but encompasses also many sectors and even social sub-systems such as the economy, research and politics. However, it is restricted to research activities and their organization. Apart from the certifications for textiles and the IG-DHS code of conduct, all voluntary measures are characterized by an openness concerning the fields of application of nano-technology. With respect to the registration of industrially produced nanoparticles, a trend towards the establishment of a mandatory system (register) can be observed. This dossier (pdf) gives an overview of the existing voluntary measures for the regulation of nanomaterial handlings.

PAPER: Titanium oxide shell coatings decrease cytotoxicity of ZnO nanoparticles

Although nanozinc oxide (nano-ZnO) is applied widely in photocatalysts and gas sensors and in biological fields, it can cause serious oxidative stress and DNA damage to mammalian cells. The researchers' aim in this study was to reduce the cytotoxicity of nano-ZnO by coating it with a TiO_2 layer.
doi: 10.1021/tx1001892

PAPER: Risk assessment of eye exposure of quantum dots

The cornea is a potential route of exposure and drug administration for nanoparticles. In this work, researchers use noninvasive two-photon microscopic imaging to study the distribution and permeability pathway of CdSe/ZnS core/shell quantum dots (QDs) capped with three different functional groups through the cornea. An *in vitro* cytotoxicity test using bovine corneal stromal cells incubated individually with all three kinds of QDs indicates that the cell viability decreases significantly as the QD concentration and incubation period increased. doi: 10.1021/tx100376n

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OPTIMIZING THE BENEFITS OF NANOTECHNOLOGY WHILE MINIMIZING AND CONTROLLING THE RISKS

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