



Gradient CORPORATION

EH&S Nano News

Volume 1, No. 9

www.ehsnanonews.com

October 2006

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Recent Government Briefs

National Nanotechnology Initiative: Supplements to the President's FY 2007 Budget

- On August 9, the Food and Drug Administration (FDA) announced the formation of an internal FDA Nanotechnology Task Force that will determine regulatory approaches that encourage the development of innovative, safe, and effective FDA-regulated products that use nanotechnology. The Task Force will recommend ways to address existing knowledge or policy gaps so that possible adverse effects of FDA-regulated products employing nanotechnology can be appropriately addressed. Innovative ways to use nanotechnology in the production of safe and effective drugs, biologics, devices, foods, feeds, and cosmetics, will be encouraged by the task force. A public meeting, chaired by the Task Force, will be held on October 10th. To gain a better understanding of developments in the field of FDA-regulated nanotechnology products and initial findings and recommendations of the meeting will be submitted to the Acting Commissioner within nine months of the event. Importantly, the Task Force will continue to foster collaborations with other federal agencies, industry, consumers, health care professionals, international organizations and other stakeholders, so that information regarding nanomaterials that could potentially be used in FDA-regulated products, is gathered effectively. For more information, visit: <http://www.fda.gov/bbs/topics/NEWS/2006/NEW01426.html>

Reports, Reviews, White Papers, and Books

White Paper on Nanotechnology Risk Governance: International Risk Governance Council

By Ortwin Renn and Mike Roco, with Annexes by Mike Roco and Emily Litten

http://www.irgc.org/irgc/_b/contentFiles/IRGC_white_paper_2_PDF_final_version.pdf#search=%22White%20Paper%20on%20Nanotechnology%20Risk%20Governance%20%22

The International Risk Governance Council (IRGC) is a non-profit organization based in Geneva and this White Paper is a result of their project, "Addressing the need for adequate risk governance approaches at the national and international levels in the development of nanotechnology and nanoscale products." The authors intend this document to be a presentation to decision-makers of an approach to analyze and manage the risks, challenges, and opportunities of nanotechnology and they also highlight deficiencies that exist in various parts of the nano field (e.g., in EH&S and risk communication) and high-level recommendations are provided. With respect to institutional recommendations, for example, the authors call for non-proprietary information on test results, impact assessments, and their interpretations on the Internet, a systematic liaison between industry and government, and incentives for both promoting and sustaining international cooperation.

Defra Consultation On a Voluntary Reporting Scheme for Engineered Nanoscale Materials: Summary of Findings and Government's Response

<http://www.defra.gov.uk/corporate/consult/nanotech-vrs/index.htm>

The UK Department for Environment, Food and Rural Affairs (Defra) published a consultation in March of this year seeking feedback on a proposal for a Voluntary Reporting Scheme for engineered nanoscale materials. The aim of the proposed reporting scheme is to "develop a better understanding of the properties and characteristics of different engineered nanoscale materials," in order to then consider potential exposures, hazards, and risks. The document was sent to 120 stakeholders and the 12-week consultation period yielded 37 responses. A summary of the responses received by Defra can be found at the link provided. In response to the key stakeholders' comments, the UK government said that it is their intention to launch the scheme this Fall and that they will provide quarterly feedback on the Voluntary Reporting Scheme to all participants and stakeholders.

Upcoming Meetings and Conferences

Lux Executive Summit Commercializing Nanotechnology

Cambridge, MA, Oct. 16, 2006

www.luxexecutivesummit.com

Lux's Executive Summit is the premiere event for those in the nanotech business. The second annual meeting focuses on commercialization and the business and finance issues that are key to any nanotech venture. Gradient is pleased to be sponsoring the Lux Summit for the second year in a row. On the afternoon of October 16, Dr. Barbara Beck, Gradient principal and nanotechnology, toxicology, and risk assessment practice leader will present a session entitled, "Linking Nanotechnology Risk Assessment with New Product Development." Several other sessions closing out the second day of the Summit address nanotechnology EH&S issues, trends, and research.

2006 US EPA STAR Nanotechnology Environmental Implications Progress Review Workshop

Arlington, VA, Nov. 13-14, 2006

<http://es.epa.gov/ncer/events/>

Researchers that have received grants through the US EPA Science to Achieve Results (STAR) program, and whose work involves the environmental implications of nanotechnology, will present their work at this upcoming event. The meeting is meant to serve as a progress assessment of STAR-funded work relevant to "the potential fate, transport, transformation, exposure, and human and eco toxicity of engineered nanomaterials" – and the organizers also hope it will instigate discussion and collaboration. The meeting is open to those in academia, government, industry, and the general public.

The 3rd International Congress of Nanotechnology (ICNT 2006) : Road Map for the Next Frontier

San Francisco, CA, Oct. 30 - Nov. 2, 2006

http://www.nanotechcongress.com/#The_3rd_International_Congress_of_Nanotechnology

This meeting for scientists and corporate executives alike will cover a far-reaching list of topics including environmental impacts, intellectual property, and intellectual standards. The format will include symposia, panels, workshops, and an open public forum and debate on "Nano Economy." Highlights of the meeting will include working groups and forums on nanotoxicology, nano ethics, and emerging nanotech companies.

Hot-off-the-Presses Peer-Reviewed Research Articles of Note

Hansen T *et al.*, 2006. "Biological tolerance of different materials in bulk and nanoparticle form in a rat model: sarcoma development by nanoparticles." *J. R. Soc. Interface*. Published Online. DOI: 10.1098/rsif.2006.0145.

Abstract: [http://www.journals.royalsoc.ac.uk/\(42441xyfc4hnz445nh3t1lys\)/app/home/contribution.asp?referrer=parent&backto=issue,17,26;journal,1,11;linkingpublicationresults,1:111337,1](http://www.journals.royalsoc.ac.uk/(42441xyfc4hnz445nh3t1lys)/app/home/contribution.asp?referrer=parent&backto=issue,17,26;journal,1,11;linkingpublicationresults,1:111337,1)

Synopsis:

- A rodent-implantation model was used to study the pathobiological impact of five different materials, namely, titanium dioxide (TiO₂), silicon dioxide (SiO₂), nickel (Ni), cobalt (Co), and polyvinyl chloride (PVC), administered either in nanoparticle or bulk form. The five test materials were selected based on their biocompatibility properties. Ni and Co have the capability of corroding, while TiO₂ and SiO₂ are ceramic materials that are relatively inert. PVC is also an inert material.
- Male rats (10 per material, per type) were implanted bilaterally (with respect to the vertebral column), with either the nanomaterial (intramuscularly) or the bulk form (subcutaneously). According to the authors, the nanomaterials had to be implanted intramuscularly instead of subcutaneously, in order to restrict the materials to an enclosed area and thus facilitate histological examinations. Rats implanted with TiO₂, SiO₂, or PVC were exposed for either 6 or 12 months. Animals implanted with Ni or Co, died or were sacrificed within four to eight months of exposure due to the formation of debilitating tumors. At the end of the exposure period, the animals were autopsied and examined macroscopically and histologically.
- A thin fibrous capsule surrounding the implantation site was observed in animals implanted with TiO₂, SiO₂, or PVC bulk material. A moderate inflammatory response was also observed in tissues surrounding the implanted bulk material and implanted SiO₂ nanoparticles. No granulomas (small nodular inflammatory lesions) were observed at the implantation site, in these animals.
- In contrast, granulomas were observed at the site of the TiO₂ and PVC nanomaterial implantation. Fibroblastic proliferation was also observed in the animals implanted with the PVC nanomaterial after 12 months of exposure.
- In animals exposed to the bulk form of Co, inflammation and preneoplasia were observed after six and eight months of exposure, respectively. Animals exposed to the nanomaterial form of Co exhibited neoplasia after six months and malignant tumors after eight months of exposure.
- The TiO₂ particles exhibited negative zeta potentials (or charge) in both cell culture media and physiological buffer.

Implications:

- These experiments are the first to evaluate the pathobiologic effect of five different materials in nanomaterial and bulk form, placed in direct contact with subcutaneous and muscular tissues.
- The authors demonstrated that, in this experimental model, it was not the physical form (nanomaterial vs. bulk) of the materials, but rather the chemical nature, that determined their toxicity. For example, Ni and Co are known to have carcinogenic properties in laboratory animals and thus elicited

these responses in the test animals when introduced in either the nanomaterial or the bulk form. In contrast, TiO₂, SiO₂, and PVC did not cause cancer in the test animals when introduced in either form.

- The authors of this study state that although neoplasias were observed in animals exposed to Ni or Co in the current study, these results should be critically evaluated for human exposures since comparable neoplasias are not found in humans. In addition, malignant transformations could not be reproduced in the sheep model that had been subject to the same experimental protocol as the rats.

Borm PJA *et al.*, 2006. "The potential risks of nanomaterials: a review carried out for ECETOC." Particle and Fibre Toxicology. 3:11.

Abstract: <http://www.particleandfibretoxicology.com/content/pdf/1743-8977-3-11.pdf>

Synopsis:

- This article provides an overview of the major applications of nanotechnology and the most recent results pertaining to risks associated with exposures to nanoparticles. The authors discuss the current nanotechnology market, unique physico-chemical characteristics of nanoparticles, sources of nanoparticles, the potential for exposures to nanomaterials, toxicity of nanoparticles, and the environmental impacts of nanomaterials.
- The nanotechnology market consists of three segments: nanomaterials, nanotools, and nanodevices. Nanomaterials consist of components between 1 and 100 nm and include nanoparticles, nanofibers, and nanotubes. Nanotools are tools and techniques that are used in synthesis of nanomaterials, manipulation of atoms, fabrication of device structures, and measurement and characterization of materials and devices at the nanoscale level.
- Sources of nanoparticles are divided into unintentionally and intentionally produced nanoparticles. The major sources of unintentionally produced nanoparticles are road transport and combustion processes. Sources of intentionally produced nanoparticles include pigments, resins, cosmetics, and other products.
- The unique properties of nanoparticles are dependent on size, composition, surface area, and the ability of nanoparticles to disperse/aggregate. Dispersion/aggregation of nanoparticles are determined by their mode of synthesis (milling, gas-phase, or wet-phase) and more importantly, surface modification of the nanoparticles after synthesis. The authors discuss the various techniques used to assess the surface properties of nanoparticles.
- Exposures to manufactured nanoparticles can occur either during the production, use, or release of the nanomaterials into the environment. Workers may be exposed to the nanoparticles at the production phase, when the nanomaterials are being synthesized, treated, or processed. The potential of exposures to nanoparticles are determined by probability of exposure, extent of exposure (time and concentration), and uptake route (inhalation, dermal, ingestion).

- Studies to date suggest that nanoparticles such as TiO₂ can enter the systemic circulation after oral or inhalation exposures, and reach several organ systems such as the lungs, liver, and brain. The dermal pathway, however, is not a major route of exposure to nanoparticles.
- Major factors affecting nanoparticle toxicity are particle number and size, dose, surface coatings, weathering and aggregation of nanoparticles, surface charges, and method of particle synthesis.
- Animal data suggest that nanoparticles are able to cause acute and chronic effects in the lungs such as inflammation and exacerbations of asthma, albeit at very high particle concentrations. Lung tumor formation was observed only in rats, and might be related to overload conditions. An increased risk of lung cancer was not observed in humans exposed occupationally to TiO₂. One of the mechanisms through which nanoparticles exert their toxic effects is through reactive oxygen species (ROS) generation.
- Data on the environmental impacts of nanomaterials suggest that they are moderately toxic to sensitive aquatic species (*e.g.*, *Daphnia magna*) and not toxic to other species such as the largemouth bass. Several studies have reported on the bactericidal properties of fullerenes or modified fullerenes. Nanomaterials are increasingly being used in the bioremediation of contaminated media.

Implications:

- There is a need for the standardization of the nomenclature system for nanomaterials/nanotechnology, to facilitate risk analysis and communication, methods for sampling and measurements, and legislation and regulation.
- Improvements are needed in areas of nanoparticle exposure and characterization methods. The authors suggest making these improvements by (a) reaching international agreement on particle parameters in occupational settings, (b) developing and using novel particle measurement techniques used in exposure measurements, (c) developing personal samplers for nanoparticles since such devices do not currently exist, and (d) developing models describing the dispersion and transformation of nanoparticles.
- Since no systematic approach currently exists to assess the probability of exposure to nanoparticles/nanomaterials, the authors recommend that an extensive review of current production practices be conducted to collect such data. The authors recommend measuring number concentrations of nanoparticles as opposed to measuring mass concentrations as a metric of exposure to nanoparticles.
- Current animal data suggest that nanoparticles can enter the systemic circulation through the ingestion and inhalation pathways. Available data suggests that human health risks from dermal exposures to nanoparticles, such as to metal oxides in sunscreens, is likely to be low.
- Studies should be conducted to gather information on the bioaccumulation, biotoxicity, and biodegradation of nanomaterials, since the production and disposal of nanomaterials into the environment continues to grow.

Guest Contributor

ABA SEER'S Review of Existing Laws and Nanotechnology - By Lynn L. Bergeson¹

Earlier this year, the American Bar Association (ABA) Section of Environment, Energy, and Resources (SEER) offered to brief representatives of the US Environmental Protection Agency's (EPA) Office of General Counsel on legal and regulatory issues arising in connection with the application of existing statutory and regulatory authorities to engineered nanoscale materials. SEER prepared briefing documents on each statute, and a separate briefing document on innovative governance mechanisms. Each document identifies the legal and regulatory issues EPA will likely encounter as it considers how best to address issues arising in connection with nanotechnology. All seven briefing documents, which are solely the product of SEER and do not purport to represent the opinions of EPA, are available at <http://www.abanet.org/environ>.

These papers provide the first comprehensive review of these federal statutes with a view toward assessing their utility in addressing the legal and regulatory issues presented by nanotechnology. The papers conclude that these core environmental statutes provide EPA with broad legal authority to address the challenges EPA is encountering as it assesses the potential risks and benefits associated with engineered nanoscale materials.

The briefing document that has generated the most interest is the paper on the Toxic Substances Control Act (TSCA). This briefing document concludes that nanomaterials include chemical substances and mixtures that EPA has authority to regulate under TSCA, that if a new chemical substance is manufactured at the nanoscale, it is subject to TSCA Section 5 premanufacture notification (PMN) requirements applicable to any new chemical substances, and that EPA may regulate nanomaterials as existing chemical substances under its TSCA Section 5(a)(2) authority to issue significant new use rules (SNUR).

Shortly after the briefing documents were posted on-line, Environmental Defense (ED) responded to the paper with its own paper dated August 31, 2006, which is available at the SEER website noted above. ED's comments reiterate its position that TSCA distinguishes "molecular identity" from "chemical structure" and that "EPA has long considered more than chemical structure where that alone is insufficient to define a substance." The SEER document notes that distinguishing between chemically similar materials on the basis of morphology presents challenges, and notes that "the discussion of EPA's legal authority under TSCA to regulate nanomaterials, whether as "new" or "existing" ... should be conducted with an understanding of the technical difficulties in distinguishing between nanoscale and conventional-sized materials of the same molecular identity."

The SEER briefing document and ED's response (and additional papers referenced in each document) are not intended to resolve the thorny issues with which EPA's TSCA office is now struggling to resolve. They provide, however, much needed detail and thoughtful consideration of these issues. Readers are urged to review and consider all sides of this interesting

debate, and be prepared to provide comment to EPA when (and if, as promised) it issues guidance on the regulation of engineered nanoscale materials under TSCA.

¹ Lynn L. Bergeson is managing director of Bergeson & Campbell, P.C., a Washington, D.C. law firm focusing on conventional and engineered nanoscale chemical, pesticide, and other specialty chemical product approval and regulation, environmental health and safety law, chemical product litigation, and associated business issues, and President of The Acta Group, L.L.C. and The Acta Group, EU, Ltd. with offices in Washington, D.C. and Manchester, UK. Ms. Bergeson served as Chair of the ABA SEER when the Nano Project was completed.

Coming Next Month

- New research on the biological mechanism of nanoparticle-mediated lung inflammation and enhancement of lung inflammation related to bacterial endotoxin



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