



# Gradient CORPORATION

# EH&S Nano News

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Editor: Barbara D. Beck, Ph.D., DABT  
Dr. Beck directs Gradient's nanotechnology, toxicology, and risk assessment practices.

## Recent Government Briefs

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

- (NSTC) On July 17, as a supplement to the President's budget for fiscal year 2007, the National Science and Technology Council released the annual report of the multi-agency National Nanotechnology Initiative (NNI). With the NNI now in its sixth year, this report summarizes the programs and activities taking place across all of the 25 agencies currently participating in the NNI, and provides details on the proposed budget for 2007. Out of a total 2007 NNI budget request of nearly \$1.7 billion for nanotechnology R&D across the federal government, approximately \$44 million is targeted primarily for environmental, health, and safety (EH&S) R&D, up 14% from the 2006 requested funding level. Notable EH&S related activities highlighted in the report include ongoing work by the Nanotechnology Environmental and Health Implications Working Group to prepare a document identifying EH&S research needs to support risk assessment of nanoscale materials, products, and processes. The report also highlights the expanded joint extramural research program between EPA, NSF, NIOSH, and NIH to address potential EH&S implications of nanotechnology for human health and the environment. In addition, the report notes the recent interagency agreement between NIOSH and DOE to investigate the impact of new diesel engine NOx and soot emission controls on the toxicity of emitted nanoparticles. For more information, see: [http://www.nano.gov/NNI\\_07Budget.pdf](http://www.nano.gov/NNI_07Budget.pdf)

### 'Nanoscience and Nanotechnologies: Opportunities and Uncertainties'

- (UK CST) The UK Council for Science and Technology (CST), the government's top-level advisory board on science and technology policy issues, recently made available a Call for Evidence soliciting written comments on the UK government's progress in meeting its commitments in nanotechnology policy. The independent review will focus on the government's actions over the past two years following its response to the Royal Society/Royal Academy of Engineering report "Nanoscience and

nanotechnologies: opportunities and uncertainties." CST is seeking comments on the timeliness and effectiveness of actions taken by the UK government. In addition, the Council is also interested in comments concerning whether recent developments in nanoscience/nanotechnology have resulted in new policy issues not previously addressed in the government's response and meriting further governmental activity. Written submissions are due by October 2, 2006, with plans for the full review to be published in Spring 2007. For more information, see: <http://www2.cst.gov.uk/cst/business/files/nano-call-for-evidence1.doc>

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## Reports, Reviews, White Papers, and Books

### Nanotechnology: A Research Strategy for Addressing Risk

By Andrew D. Maynard, Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies

[http://www.wilsoncenter.org/index.cfm?topic\\_id=166192&fusaaction=topics.event\\_summary&event\\_id=194810](http://www.wilsoncenter.org/index.cfm?topic_id=166192&fusaaction=topics.event_summary&event_id=194810)

This report synthesizes much of the scientific and policy discussions currently going on with respect to nanotechnology risk research – and provides specific recommendations for what should be done next. Dr. Maynard calls for a "top-down, authoritative oversight of strategic risk-based research," where federal agencies should both carry out the research and provide adequate funding for "highly relevant" work. He prioritizes risk research needs over the next 10 years, and also breaks down short-term research goals by federal agency. In addition, Dr. Maynard stresses the need for a new interagency group to design and implement the research strategy. While he notes that some of what he recommends will not be agreeable to all involved in the nano industry, he asserts that risk research is needed to assure that economically viable technologies and products can be produced, without threat of harming people, animals, or the environment. He concludes that while many data gaps still exist with respect to risk research, enough is currently understood to know that some nanomaterials and products will pose a distinct risk to human and environmental health in comparison to conventional materials.

## American Bar Association, Section of Environment, Energy, and Resources Nanotechnology Project

<http://www.abanet.org/environ/nanotech>

The American Bar Association (ABA) Section of Environment, Energy, and Resources (SEER) has recently made available the results of their review of the six core federal environmental statutes (*e.g.*, CERCLA, TSCA) and the statutes' applicability to nano EH&S issues. The Section's findings – produced in seven reports – have been presented to US EPA representatives over the last several months. SEER explains that, in general, “the papers concluded that the core environmental statutes were found to provide EPA with sufficient legal authority to address adequately the challenges EPA is expected to encounter as it assesses the enormous benefits of and potential risks associated with nanotechnology.”

## Nanotechnologies for Environmental Cleanup

By Paul G. Tratnyek and Richard L. Johnson

<http://cgr.ebs.ogi.edu/iron/TratnyekJohnson06.pdf>

Tratnyek and Johnson provide an important addition to the scientific literature on remedial nanotechnology. The authors specifically discuss the use of nanoscale zero-valent iron (NZVI) to remediate groundwater and they address three topics that are often raised when the potential risks of this technology are considered: morphology, reactivity, and mobility of the NZVI. This review paper provides up-to-date information on these aspects of NZVI and discusses the data gaps that remain. In all, while the authors are well aware of the many questions regarding *in situ* applications of NZVI, they conclude that the materials used for such applications “are not as small, reactive, persistent, or mobile” as most of the materials for which there is specific evidence of potential human or ecological risk.

## Upcoming Meetings and Conferences

### Nanotechnologies: Safety for Success

Helsinki Region, Finland, Sept. 14-15, 2006

<http://www.fmnt.fi/ntss/>

Safety and risk issues associated with nanotechnology are at the center of this international conference. Attendees will gain a solid understanding of the many topics and concerns associated with nanotechnology's known, unknown, and potential risks through talks as well as a breakout session. The program includes sessions on whether changes are needed in the existing regulatory framework and how to better communicate with the public to improve perception of nanotechnology and its products. The underlying theme of this meeting is how a focus on safety can improve the competitive edge for nanotechnologies.

## Lux Executive Summit: Commercializing Nanotechnology

Cambridge, MA, Oct. 16 - 17, 2006

[www.luxexecutivesummit.com](http://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. This two-day meeting is also a unique networking opportunity where senior executives, leading scientists, policy makers, and investors will all come together.

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, and promise to be interesting and informative.

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

**C.M. Sayes, *et al.* 2006. “Correlating nanoscale titania structure with toxicity: a cytotoxicity and inflammatory response study with human dermal fibroblasts and human lung epithelial cells.” *Toxicological Sciences*. 92 (1): 174-185.**

**Abstract:** [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=16613837&query\\_hl=2&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16613837&query_hl=2&itool=pubmed_docsum)

Synopsis:

- Phase composition, and its relationship to reactive species (RS) generation, is a desirable property of titania nanocrystals that has been exploited in applications ranging from self-cleaning glass to low-cost solar cells. This article summarizes research conducted to investigate how the chemical properties of titania nanocrystals, and specifically their phase composition, correlate to *in vitro* toxicological effects. Nanotitania samples chosen for study were the anatase and rutile forms of titanium dioxide, commonly manufactured crystalline forms of titanium dioxide which differ in their phase composition and photocatalytic properties.
- Nanocrystalline titanium dioxide (nano-TiO<sub>2</sub>) samples of controlled phase composition were generated using state-of-the-art hydrothermal methods, and *in vitro* cytotoxicity screening assays with two human cell lines (human dermal fibroblasts and human lung epithelial cells) were used to assess their biological effects under ambient conditions (*e.g.*, no significant light illumination). Among the forms of nanoscale titania evaluated in the study were anatase, rutile, and anatase/rutile particles, each with sizes in the range of 3-10 nm and exposure concentrations ranging from

3 mg/mL to 3 mg/mL. Biochemical endpoints included cell viability, membrane leakiness (via lactate dehydrogenase, or LDH, release), mitochondrial activity, and inflammation (via IL-8 production).

- Compared to other nanoparticle systems such as fullerenes, all of the nano-TiO<sub>2</sub> samples were found to be of relatively low toxicity, with cytotoxicity and inflammation only occurring for relatively high concentrations (100 mg/L). Classic dose-response curves were observed, with time course experiments showing greater toxicological effects with increased time of exposure.
- In contrast to other recent nanoparticle studies, no correlation was observed between biological responses and sample surface area, with smaller nano-TiO<sub>2</sub> eliciting effects comparable to larger nano-TiO<sub>2</sub>, through phase composition was found to correlate strongly with cytotoxicity. Anatase particles were reported to be the most toxic to human cells in culture and nano-TiO<sub>2</sub> rutile particles were the least toxic.
- Measurements of *ex vivo* reactive oxygen species generation confirmed that the most cytotoxic nano-TiO<sub>2</sub> species were also the species most effective at generating RS species under light illumination.

#### Implications:

- As discussed by the authors, their data suggest that nano-TiO<sub>2</sub> species optimized for RS production in photocatalysis are also more likely to generate damaging RS species in cell culture.
- Results show some similarities and differences in the cytotoxicity of nano-TiO<sub>2</sub> species compared to other test nanoparticles. Notably, similar to findings for other engineered nanoparticles as well as ambient ultrafine particles, these results are suggestive of the role of oxidative damage in the biological mechanism of cell damage for nano-TiO<sub>2</sub>. While of lower overall toxicity than other tested nanoparticle species, results from these screening assays demonstrate that nano-TiO<sub>2</sub> species differ from species such as aggregated fullerenes in their apparent capability to disrupt cellular mitochondrial activity.
- The authors conclude that their results highlight the potential role of *ex vivo* measures of RS production for cytotoxicity screening.

#### **K. Donaldson, *et al.* 2006. “Carbon nanotubes: a review of their properties in relation to pulmonary toxicology and workplace safety.” *Toxicological Sciences*. 92 (1): 5-22.**

**Abstract:** [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=16484287&query\\_hl=4&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16484287&query_hl=4&itool=pubmed_docsum)

#### Synopsis:

- In light of projections of increased manufacture and potential human exposures to carbon nanotubes (CNT), this article reviews the state of the toxicological knowledge for carbon nanotubes and examines the relevance of currently available toxicological paradigms for fibers and nanoparticles to the toxicity of inhaled CNT. In addition, the authors summarize

workplace regulations applicable to airborne CNT exposures and discuss implications of our current understanding of CNT toxicity on workplace regulation.

- Based on their literature review, the authors conclude that there is toxicological evidence suggesting that CNT may have unusual toxicity properties. In particular, the authors highlight research indicating that CNT have a special ability to stimulate mesenchymal cell growth and to cause granuloma formation and fibrogenesis.
- The authors cite several studies that have shown more adverse effects for CNT than for the same mass of carbon black nanoparticles and quartz.
- Although no studies have currently evaluated the toxicity of CNT with lengths greater than 20 mm, the authors hypothesize that “long CNT” can cause the same types of pathology that long biopersistent fibers such as mineral and synthetic vitreous fibers (SVF) cause in rats and humans at sufficient fiber numbers.
- The authors highlight research indicating that CNT may exhibit some of their effects through oxidative stress and inflammation, with proinflammatory potential related to their surface area as has been found for nanoparticulate carbon black and a range of low-toxicity, low-solubility particles.

#### Implications:

- With available research findings showing that nanotubes have characteristics of both conventional fibers and nanoparticles, the authors propose that two types of toxicologic strategies need to be developed for CNT, one for “long CNT” that behave like fibers and one for “short CNT” that behave like proinflammatory nanoparticles.
- The authors highlight the absence of any inhalation studies of nanotubes and the pressing need for these studies that can overcome some of the limitations of the instillation exposure procedures, including unrealistically high dose and dose rates and the potential for artifactual effects due to formation of large mats and aggregates.
- With respect to workplace regulation of long, fibrous CNT, the authors conclude that conventional fiber counting, as currently applied to mineral fibers, is not practical for determination of airborne CNT. They suggest that methodologies need to be developed for use of Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) for routine assessment of CNT levels in workplaces.
- Given toxicological studies linking CNTs with mesenchymal cell growth, granuloma formation, and fibrogenesis, there is limited evidence of the carcinogenic potential of CNTs, and Donaldson *et al.* recommend that chronic studies of CNT toxicity emphasize carcinogenic and mesothelioma endpoints in the lung.
- The authors conclude that translocation of CNT throughout the body, and particularly to the pleura, is clearly a potentially important process requiring focused research.

## Guest Contributor

### A Stage-Gate Solution to Nanotech Environmental, Health, and Safety Risks

Michael W. Holman, Ph.D., Lux Research

The potential EH&S risks of nanomaterials challenge companies looking to take advantage of nanotechnology. At Lux Research, we hear many stories about promising research projects scuttled, productive collaborations abandoned, and next-generation product ideas shelved – all because firms aren't sure how to manage nanomaterial EH&S issues.

Would-be nanotech developers struggle with three aspects of the problem. First, many can't get a good handle on the real risks nanomaterials might present, due to a lack of data and the costs of funding new studies. Second, many look at recent events like protests in France over the opening of a nanotech research center, and worry about the perceived risk of nanomaterials – the risk that the public might come to fear anything labeled “nano” – regardless of real risks. Finally, firms are also tempted to delay or abandon nanotech efforts because of worries about regulations, and the uncertainties remaining about how, for instance, the EPA will handle nanomaterials under the Toxic Substances Control Act (TSCA).

Fortunately, there are clear steps firms can take to confront all of these challenges. Companies working in nanotech can put processes in place to manage real risks, create communication strategies to limit their exposure to perceptual risks, and make projections about the emerging regulatory environment to set appropriate planning assumptions. However, to balance the need for safety with economic reality, firms that use nanomaterials will need to implement these plans judiciously. Companies clearly can't afford to do exhaustive testing on every nanomaterial their scientists experiment with in the lab, but those that wait until just before product launch to consider EH&S concerns will find themselves burned badly and often.

The solution is to match appropriate action to each stage of product development – a “stage-gate” approach. Take a hypothetical example, the use of carbon nanotube (CNT) composites for engine turbine blades at a company like General Electric. When the project is first proposed, planners can review known data from the literature and survey the current state of relevant regulations. As research progresses, simple *in vitro* tests can alert the team if the particular CNT variants it's using seem to present elevated risks, while marketers evaluate the sensitivity of target customers to EH&S issues. When products begin to move into development, the firm can take advantage of industry consortia to pursue more testing, and begin to communicate with regulators. As products are scaled up, final tests should be completed, and the firm should reach out to consumer groups to talk about steps that have been taken to ensure safety. Finally, once products are launched, ongoing monitoring will keep the firm on top of issues across the lifecycle, and promote the environmental benefits the products offer.

Developing products based on novel technologies always entails grappling with uncertainty. Despite the challenges, companies can overcome nanotech EH&S issues with planning and process. With a concrete approach like that outlined here, firms can ensure that they – and society as a whole – reap the benefits that safely applying nanomaterials to products will bring.

*Michael Holman is an analyst at Lux Research, the world's leading nanotech research and advisory firm. He will also be presenting on nanotech EH&S issues at the second annual Lux Executive Summit, October 16-17 in Cambridge, MA. More information at: [www.luxexecutivesummit.com](http://www.luxexecutivesummit.com)*

## Coming Next Month

- Research describing nanomaterial toxicity using a rodent implantation model
- ECETOC's latest review of potential nanomaterial risks



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