



# Gradient CORPORATION

# EH&S Nano News

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Editor:

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## Recent Government Briefs

### **The National Institute for Occupational Safety and Health (NIOSH)**

NIOSH recently announced that they will form an interdisciplinary team of NIOSH researchers in the area of nanotechnology. The NIOSH Nanotechnology Field Research Team will be comprised of research team leaders on detail from their usual duties for approximate 30-60 day periods, as well as interdisciplinary field researchers drawn from such areas as industrial hygiene, engineering, occupational medicine, and risk assessment. By partnering with employers and other research institutions, the function of the team will be to assess and obtain insight on materials, processes, current and future worker exposures, work practices, control procedures, and medical monitoring in workplaces where nanoparticles are generated or used. For more information, see: <http://www.cdc.gov/niosh/topics/nanotech/focus.html>.

### **The National Institute for Occupational Safety and Health (NIOSH)**

NIOSH has made available for comment the draft NIOSH Current Intelligence Bulletin: Evaluation of Health Hazard and Recommendations for Occupational Exposure to Titanium Dioxide. By providing a quantitative risk assessment for titanium dioxide, a poorly soluble powder that can consist of nano-sized particles, this report has some potential application to nanoparticle risk assessment. A public meeting is scheduled for February 27, 2006 in Cincinnati to discuss this draft document, with a deadline for receipt of comments of March 31, 2006. For more information, see: <http://www.cdc.gov/niosh/docs/preprint/tio2/>.

## Reports, Reviews, and White Papers

### **Managing the Effects of Nanotechnology – By Dr. J. Clarence Davies**

From a January 11, 2006 session at *The Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars*

<http://www.wilsoncenter.org/events/docs/Effectsnanotech-final.pdf>

The report, written by a renowned expert on environmental

policy and research, is a policy analysis piece on government oversight of nanotechnology. The author details why, in his view, current regulations are not adequate for nanotechnology. He then reviews the benefits of developing a new law for nanotechnology products, as well as the likely obstacles to such legislation. Further, he explores ways to encourage positive and environmentally beneficial applications of nano-

technology. This report has received considerable attention and there is disagreement among experts as to whether new legislation is warranted. Critique from E. Clayton Teague, director of the National Nanotechnology Coordination Office, can be found in the following article: <http://pubs.acs.org/cen/government/84/8405gov1.html>. He explains that it is too early to draw any conclusions on the safety of nanoparticles and that focus now must be placed on EH&S research.

### **EHS Database**

From the *International Council of Nanotechnology (ICON)*  
<http://icon.rice.edu/research.cfm>

This database consists of abstracts and citations of research papers related to the EH&S implications of nanoscale materials. This database is free and open to the public for use. Users can search for articles of interest by author, year, or by a range of topics such as 'exposure pathway,' 'particle type,' and 'method of study.' ICON, based at Rice University, is an international group that brings together industry, academia, NGOs, and governmental agencies to share resources and information. ICON's mission is to assess, communicate, and reduce the environmental and health risks associated with nanotechnology, while also promoting its sustainability and benefit to society.

## Upcoming Meetings and Conferences

### **Nano & Bio in Society – Chicago, IL: March 27-30, 2006**

*The Societal Implications of Nano and Bio Technology*  
<http://nabisconference.com/2006/>

Scientists, companies involved in nanotech, legal and financial experts, and governmental representatives will be among

### **In This Issue**

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the attendees of this conference aimed at addressing both the societal impacts of nanotech research and the role of the scientist in shaping society's future. The intent of the meeting is to bring together scientists from around the world to discuss their work in nanotech and biotech – and the societal implications of their work. The areas of concentration included in this meeting range from cosmetics to environmental applications.

### **NanoBusiness 2006 – New York, NY: May 17-19, 2006**

*The Official Conference of the NanoBusiness Alliance*  
<http://www.nanobusiness2006.com/>

This meeting will be the fifth annual for the NanoBusiness Alliance and it will explore issues in nanotechnology such as investing, commercialization, and current and future global opportunities. This gathering is intended for business leaders, investors, venture capitalists, scientists, engineers, and government officials.

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

**Sayes CM, Liang F, Hudson JL, Mendez J, Guo W, Beach JM, Moore VC, Doyle CD, West JL, Billups WE, Ausman KD, Colvin VL. 2006. "Functionalization density dependence of single-walled carbon nanotubes cytotoxicity *in vitro*." *Toxicol Lett.* **161(2):135-42.** [Link to Abstract](#)**

#### *Synopsis:*

- This article summarizes a set of *in vitro* cytotoxicity screens performed using cultured human dermal fibroblasts dosed with varying concentrations of several types of single-walled carbon nanotubes (SWNT).
- *In vitro* tests were conducted for three different water-dispersible SWNT samples, including two prepared with three different densities of sidewall functionalizations, as well as for a SWNT sample with no deliberate sidewall functionality stabilized in a surfactant solution. SWNT samples were characterized using both spectroscopic and microscopic techniques, and both viability/cytotoxicity and mitochondrial activity of the human dermal fibroblasts were assessed using commercial tests.
- Cell death did not exceed 50% for any of the experiments involving sidewall functionalized SWNTs, with sidewall functionalized SWNT samples showing substantially less cytotoxicity than the surfactant stabilized SWNTs. Only the surfactant stabilized SWNT sample was found to exhibit statistically significant cytotoxicity, despite a dose level that was more dilute than that of the sidewall functionalized SWNTs by three orders of magnitude.
- As the degree of sidewall functionalization was increased, cytotoxicity was found to decrease. Mi-

tochondrial activity was found to remain unchanged with changes in the degree of sidewall functionalization.

- Fluid atomic force microscopy (AFM) indicated that SWNTs in aqueous suspension precipitate out and selectively deposit on cellular membranes.

#### *Implications:*

- Findings from this study for SWNT samples are consistent with those reported previously for water-suspendable fullerenes, where cytotoxicity was significantly reduced as the degree of functionalization on the surface of the fullerene cage was increased. Taken together, these findings suggest that nanoparticle toxicity can be reduced through engineering of surface properties.
- These study findings are also suggestive of the potential for assessing the toxicity of different types of nanomaterials in a screening manner.
- As noted by the study authors, their microscopic observations indicating "significant interactions of SWNTs with biomembranes" are promising from the perspective of the development of the bio-nano interface for drug delivery and diagnostic applications.

**Kim JS, Yoon TJ, Yu KN, Kim BG, Park SJ, Kim HW, Lee KH, Park SB, Lee JK, Cho MH. 2006. "Toxicity and tissue distribution of magnetic nanoparticles in mice." *Toxicol Sci.* **89(1):338-47.** [Link to Abstract](#)**

#### *Synopsis:*

- This article summarizes a set of *in vivo* and *in vitro* laboratory experiments designed to evaluate the biological distribution and potential toxicity of magnetic nanoparticles (MNPs).
- *In vivo* experiments were conducted using water-soluble silicon-overcoated MNPs, with potential life science applications such as drug/gene delivery and bioimaging, as the model nanoparticles. In 4-week experiments, mice were exposed intraperitoneally (*i.e.*, through injections into the abdominal wall) to either 100, 50, 25, or 10 mg/kg (blood-brain barrier tests only) MNPs.
- MNPs were found to be distributed throughout the body, with distribution occurring in all organs (brain, liver, lungs, kidneys, spleen, heart, testes, and uterus) and exhibiting a time-dependent pattern. Distribution in the lung was found to differ from that in other organs, as almost negligible amounts of MNPs were found in the lungs.
- Despite their widespread distribution, investigators reported no abnormal clinical signs (*i.e.*, no adverse effects on growth, or abnormal clinical signs or behaviors) or apparent toxicity (as measured in a battery of tests, including blood brain barrier permeability, *in vivo* serum biochemical analysis, blood chemistry, histopathological examination, and *in vitro* mutagenicity assays) for any of the MNPs exposure levels.

*Implications:*

- Given that the MNPs were found to penetrate both the blood brain barrier as well as the blood-testis barrier with little apparent evidence of toxicity, the authors concluded that the MNPs exhibited good biological characteristics and showed potential as promising vectors for gene transfer and gene/drug delivery.
- Due to the ability of the MNPs to penetrate the blood brain barrier and to biopersist in the body over time, the authors recommended the need for long-term studies to clarify the potential chronic toxicity of MNPs.
- Given different tissue distribution of MNPs, in particular to the lungs, kinetic models may be of use in modeling their behavior (or dose) in different organs.
- However, the use of intraperitoneal instillation as an exposure method makes extrapolation of these findings to more typical exposure pathways (*i.e.* ingestion, dermal contact, inhalation) highly uncertain.

## Guest Contributor: Melissa Hoffer, Esq.

### Regulation of Nanomaterials in the U.S.

The Toxic Substances Control Act (TSCA) regulates the manufacture and use of “chemical substances,” a term of art that includes existing chemical substances (those listed on the TSCA Inventory), new chemical substances (any substance not on the TSCA Inventory), and significant new uses (SNU) (designated by EPA by rule) of chemical substances. TSCA imposes notice, recordkeeping and reporting requirements on manufacturers and importers. Manufacturers of new chemical substances are required to provide certain data to EPA in advance of commercial manufacturing (Pre-Manufacture Notice or PMN), including health / environmental effects studies in the manufacturer’s possession and control. Any other health studies known to the manufacturer concerning such effects must be described in the PMN. There are several exemptions to the PMN requirement potentially available to nanomaterial manufacturers (and those who incorporate nanomaterials into their products). For example, the Low Volume / Low Release (LVE) (substances produced in quantities of 10,000 kg or less per year) and Low Release and Exposure (LoREX) (production results in extremely limited human/environmental exposure) exemptions provide an abbreviated PMN notice and review period.

In September 2005, EPA approved manufacture of a certain carbon nanotube (CNT) under the LoREX exemption and required the manufacturer to produce the chemical under certain conditions, including allowing EPA to review and authorize continuing manufacture. EPA’s action illustrates that, presently, it is evaluating nanomaterials on a case by case basis, as it would any other substance. The decision

also suggests that EPA may treat nanomaterials whose bulk form (carbon, in the case of CNTs) is already listed on the TSCA Inventory as “new chemical substances.” However, the question whether a nanoscale form of an existing chemical constitutes a “new chemical substance” for purposes of TSCA remains open until EPA issues a definitive interpretation.

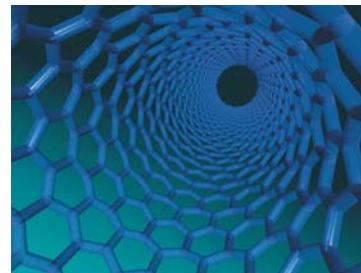
Other federal environmental statutes, including the Clean Air Act, National Environmental Policy Act, and Resource Conservation and Recovery Act, could apply to engineered nanomaterials. EPA has not yet clarified whether and how those frameworks will apply. State laws, such as California’s Safe Drinking Water and Toxic Enforcement Act of 1986 (Prop 65), requiring manufacturers to label products containing substances known to cause cancer or reproductive toxicity, may also apply.

Nanomaterials currently are not regulated as a class under the Occupational Safety and Health Act, but may be subject to OSHA standards applicable to the bulk form of the material (*e.g.*, nuisance dust). In October 2005, NIOSH issued voluntary guidance on protecting worker safety, “Approaches to Safe Nanotechnology, An Information Exchange with NIOSH.”

Voluntary nomenclature and environmental safety and health standards currently being developed by the American Society for Testing and Materials (ASTM) and the International Standards Organization (ISO) will very likely be incorporated into regulatory schemes and will have a substantial effect on the development of nanotechnologies in the U.S. and internationally. Stakeholders should actively monitor or participate in the standards-development process.

The success of promising new nanotechnologies will turn on public confidence, built on science-based transparent regulation. Manufacturers should be aware of regulatory developments, prepare for public debate on the issues of regulation and responsible development, and take common sense precautions until more is known about potential health and environmental effects posed by nanomaterials.

*Melissa Hoffer is a Junior Partner with Wilmer Cutler Pickering Hale and Dorr, LLP. For information about the firm’s Nanotechnology Practice Group: <http://www.wilmerhale.com/nanotechnology/>.*



## Gradient Nanotechnology Presentations

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Miami, FL. January 29-February 1, 2006. Barbara D. Beck and Noelle M. Cocoros. "A Qualitative Risk Assessment to Evaluate the Remediation of Trichloroethylene by Nanoscale Zero-Valent Iron Particles," presentation at the 1st International Conference on Nanotoxicology: Biomedical Aspects. [http://www.gradientcorp.com/nano/bdb\\_nano\\_poster.pdf](http://www.gradientcorp.com/nano/bdb_nano_poster.pdf)

Minneapolis, MN. October 3-6, 2005. Christopher M. Long. "Measurement, Fate, and Exposure Potential of Ultrafine Particles in Indoor Air: Lessons Learned for Nanotechnology," poster session to be presented at the 2nd International Symposium on Nanotechnology and Occupational Health. [http://www.gradientcorp.com/nano/cml\\_nano\\_poster.pdf](http://www.gradientcorp.com/nano/cml_nano_poster.pdf)

## Coming Next Month

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A recent review article by Nel et al. (2006), entitled "Toxic Potential of Materials at the Nanolevel," will be reviewed in the April issue of our newsletter. This article examines various issues related to nanotoxicology, including the particular concerns related to toxicity testing of nanomaterials.

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