



# Gradient CORPORATION EH&S Nano News

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## Recent Government Briefs

### Announcement of the NIOSH Nanotechnology Metal Oxide Particle Exposure Assessment Study

<http://www.cdc.gov/niosh/docs/2008-122/pdfs/2008-122.pdf>

The National Institute for Occupational Safety and Health (NIOSH), a part of the Centers for Disease Control and Prevention (CDC), is the leading federal agency in the US conducting research and providing guidance on the occupational safety and health implications of exposure to engineered nanomaterials. As part of its nanotechnology research agenda, NIOSH initiated a study to investigate exposure to fine (0.1 $\mu$ m to 2.5 $\mu$ m diameter) and ultrafine (<0.1 $\mu$ m diameter) metal oxides. The purpose of the study is to characterize workplace exposure to ultrafine metal oxides. The specific objectives are to: 1) characterize airborne metal oxides exposure metrics by job or process, 2) obtain quantitative estimates of exposure to fine and ultrafine metal oxides by particle size, and 3) evaluate a strategy for measuring workplace exposure to fine and ultrafine metal oxides. Manufacturers and end-users of fine and ultrafine metal oxides are being asked to participate; workers who work with these materials will also be able to participate in this study.

### Update on the US EPA Nanoscale Materials Stewardship Program (NMSP)

<http://www.epa.gov/oppt/nano/stewardship.htm>

In January 2008, US EPA launched the voluntary Nanoscale Materials Stewardship Program (NMSP), with the goal of helping to provide a firmer scientific foundation for regulatory decisions for nanoscale materials through encouraging submission and development of pertinent information including risk management practices. Under the "basic" NMSP program, participants who manufacture, import, process, or use nanoscale materials will report available information on material characterization, hazard, use, potential exposures, and risk management practices. Under the "in-depth" program, participants will voluntarily perform testing over time and work with US EPA to facilitate data development. Three participants have already made submissions to the basic program; ten others have made commitments to submit information. At this time, no companies have volunteered for the in-depth program. US EPA encourages participants in the basic program to submit existing data on or before July 28, 2008.

## Reports, Reviews, White Papers, and Books

### Nanoecotoxicology: Nanoparticles at Large

By Renata Behra, Department of Environmental Toxicology, Swiss Federal Institute of Aquatic Science and Technology, and Harald Krug, Materials-Biology Interactions, Empa Materials Science and Technology, Switzerland

<http://www.nature.com/nnano/journal/v3/n5/abs/nnano.2008.113.html>

This review article discusses three research priorities for improving our understanding of the potential environmental impacts of engineered nanoparticles that have been identified by environmental toxicologists, chemists, and social scientists. First, there is a need to prioritize the types of nanoparticles for testing in biological experiments. Given the widespread usages of some types of nanoparticles in consumer products (e.g., nanosilver embedded in commercially available socks), some nanoparticles have a greater potential for environmental release. Second, routes of uptake by organisms in different environments need to be examined, especially given that nanoparticle uptake can vary based on cell size and shape and the fact that some nanoparticles may biomagnify in the food chain. Last, research is needed to identify experimental organisms of the greatest relevance. It is unknown if organisms currently used to represent major trophic levels

(e.g., water fleas) can be used with nanomaterials to predict effects of the larger ecosystem. Focusing on these three areas will build a solid framework for understanding the impact of engineered nanoparticles on the environment.

### **Towards Predicting Nano-Biointeractions: An International Assessment of Nanotechnology Environment, Health and Safety Research Needs**

By the International Council on Nanotoxicology  
[http://cohesion.rice.edu/CentersAndInst/ICON/emplibary/ICON\\_RNA\\_Report\\_Full2.pdf](http://cohesion.rice.edu/CentersAndInst/ICON/emplibary/ICON_RNA_Report_Full2.pdf)

In this report, the International Council on Nanotoxicology (ICON), an extension of the National Science Foundation, proposes a framework for the development of predictive models of nanotechnology's impacts on biological systems and at the molecular level. In support of this effort, ICON held two workshops, representing academia, industry, governments, NGOs, and 13 countries. The first group discussed what is known about the key classes of nanomaterials, finding that (1) models must be developed to describe the dynamic nature of nanomaterials, (2) screening tools are needed to correlate the functional properties of nanomaterials with their potential for biological interaction, and (3) exposure assessment studies are needed to characterize nanomaterial physicochemical properties and their implications for total doses. The second group focused on identifying the research needs and milestones to inform predictions of an engineered nanoparticle's biological effects, finding that (1) quantitative models are needed to describe how the physicochemical properties of nanoparticles control the nature and extent of biomolecular interactions, (2) dose and dose rate may need to be validated independently for nanomaterials, (3) research is essential to develop better biomarkers to address the vast diversity of nanoparticle types. The product of these workshops will build on previous work toward research agendas for biointeractions of nanomaterials.

## **Upcoming Meetings and Conferences**

### **11th International Inhalation Symposium - Benefits and Risks of Inhaled Engineered Nanoparticles**

June 11 - 14, 2008, Hannover, Germany  
<http://www.inis-symposium.com/index.html>

The German Society of Toxicology and the US Environmental Protection Agency are hosting this symposium which will cover areas of current concern and active research in the context of engineered nanoparticles. Scientists from academia, government, and industry will have the chance to present and discuss active research on the ramifications of inhaled nanoparticles, including methods of measurement, pulmonary and systemic toxicity, mechanisms of action, potential sources of human exposure, and biological test systems. The symposium sessions will be led by internationally-recognized experts in the field of nanotechnology. Papers and selected

posters resulting from this symposium will be published in the journal *Inhalation Toxicology*.

### **2nd International Conference on Nanotoxicology**

September 7-10, 2008, Zurich, Switzerland  
<http://www.nanotox2008.ch>

Hosted by the University of Zurich and the Swiss Federal Institute of Technology, this conference aims to address the hazards of and exposure to nanomaterials. Participants, who will include the public and stakeholders, will have the chance to attend panels on the biological effects of nanomaterials and learn about the development of new methods and standardization processes. The conference program will cover topics such as exposure to and uptake of nanomaterials, the biological effects and mechanisms of nanomaterials, and the properties of special materials associated with nanotechnology.

### **International Environmental Nanotechnology Conference: Applications and Implications**

October 7-9, 2008, Chicago, Illinois  
<http://emsus.com/nanotechconf/index.htm>

Several US government agencies including US EPA Region V, the National Science Foundation and the Agency for Toxic Substances and Disease Registry are hosting the International Environmental Nanotechnology Conference to discuss how nanotechnology can be used in environmental cleanup applications, how nanoparticles are intentionally released into the environment for remediation purposes, and how people may be exposed to them. The conference will bring together researchers and practitioners from around the world who will provide commentary on the nanotechnology applications for remediation of environmental contaminants, the implications of releasing manufactured nanoparticles into the environment, pollution control, and nano-enabled sensing. Keynote addresses and breakout session topics will include nanomaterial toxicity, fate and transport, and biological exposure.

### **4th International NanoRegulation Conference 2008: Beyond Regulations – Voluntary Measures in Nano Risk Governance**

September 16 - 17, 2008, St.Gallen, Switzerland.  
[http://www.nanoeurope.com/wEnglisch/messen/nanoeurope/01\\_besucher/konferenzen/nano\\_regulation\\_vorschau.php](http://www.nanoeurope.com/wEnglisch/messen/nanoeurope/01_besucher/konferenzen/nano_regulation_vorschau.php)

Nano Europe and several other research organizations have focused this year's International NanoRegulation conference on voluntary measures for the identification, assessment, control, and communication of nanotechnology risks. The conference offers a platform for discussion and consensus decision-making for nanotechnology decision-makers in industry, the public, and the media. The aim is to present several concepts of voluntary measures, to discuss experiences and draw conclusions for the future. The first half of the conference will focus on design principles and experiences with voluntary measures. The second half will be devoted to the discussion of a new approach to international coordination.

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

**1. Pui, D.Y.H., et al. 2008. "Recirculating air filtration significantly reduces exposure to airborne nanoparticles." *Environ. Health Perspect. EHP-in-Press*. Abstract: <http://www.ehponline.org/docs/2008/11169/abstract.html>**

### Synopsis:

- Given emerging public health concerns regarding potential exposures to traffic-related nanoparticles, as well as questions regarding the effectiveness of traditional fine particle engineering controls for engineered nanoparticles, this study investigated the effectiveness of recirculating air filtration for removal of traffic-related nanoparticles and engineered silver nanoparticles.
- On-road tests were conducted in two commercial vehicles (a 2003 Saab 93 and a 2007 Toyota Camry) to test the effectiveness for removal of traffic-related nanoparticles of in-car air recirculation through standard cabin air filters. In addition, recirculating air filtration was evaluated in a simulation of a nanomaterial production facility, where silver nanoparticles were produced using a silver nanoparticle aerosol generation and room air was recirculated through a Viledon HVAC filter. For both scenarios, a portable condensation particle counter was used to continuously measure particle number concentrations. In addition, for in-car recirculation, measurements of time-resolved size distributions were made to assess the impacts of air recirculation on particles of different sizes.
- Despite finding that the cabin air filters were relatively inefficient at removing nanoparticles compared to HEPA filters, these researchers observed that in-cabin particle number concentrations nonetheless were reduced to levels below those of typical office environments within approximately 3 minutes for the experiments in the Toyota Camry with air recirculation on and a filter in place. Without a filter in place, air recirculation was still effective (~13 minutes to achieve reduced levels consistent with typical indoor levels) at reducing in-cabin airborne nanoparticles, suggesting that losses occurred within the ventilation and recirculation due to collection in the blower housing and cooler system.
- Air recirculation through a standard HVAC filter was also found to be effective at reducing airborne levels of engineered silver nanoparticles, with levels dropping to those of a typical office setting within about 20 minutes for the simulated nanomaterial production facility.

### Implications:

- Despite the fact that automobile cabin air filters are not generally evaluated for their filtration efficiency of particles smaller than 300 nm, these inexpensive, low-efficiency filters were found to effectively reduce

airborne nanoparticle concentrations when used in air recirculation systems. Based on a model developed by the study investigators, the particle removal efficiency increased from 19% to 45.5% in the Toyota Camry when the cabin air filter was inserted into the recirculation loop. As discussed by the study authors, air recirculation thus represents an easy-to-implement solution for reducing commuting exposures to vehicular nanoparticle emissions.

- Together with recent findings confirming the effectiveness of conventional commercial respirators for filtration of engineered nanoparticles, this study provides additional support that engineering methods developed to control exposures to other types of fine and ultrafine particles are also effective for engineered nanoparticles. With the added benefits of their low cost and technological simplicity, these findings indicate that air recirculation systems may be a viable exposure control option for nanomaterial manufacturers and users for use in other indoor environments.
- The study authors developed a predictive model for nanoparticle removal via recirculating air filtration that may have applications in aiding the further design of recirculating air filter systems for control of nanoparticle exposures.

**2. Poland, C.A., et al. 2008. "Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study." *Nature Nanotechnology. Advanced Online Publication*. Abstract: <http://www.nature.com//nnano/journal/vaop/ncurrent/abs/nnano.2008.111.html>**

### Synopsis:

- Given their nanometer-scale diameter and needle-like fiber shape, many have remarked on the structural resemblance between carbon nanotubes and asbestos. This study is one of two recent studies to report toxicological findings consistent with asbestos-like pathogenicity of carbon nanotubes, providing preliminary data for the fiber effects of long multi-walled carbon nanotubes (MWCNTs).
- In this pilot study, mice were given intraperitoneal injections containing 50 µg of one of four MWCNT samples, including two samples with a large proportion of long straight fibers longer than 20 µm and two samples consisting of CNTs arranged in low-aspect-ratio tangled aggregates. A long-fiber amosite (LFA) and a short-fiber amosite (SFA) were used as positive and negative controls, respectively, while a nanoparticulate carbon black (NPCB) sample served as a non-fibrous graphene control. Either 24-hours or 7-days post-injection, mice were killed and peritoneal (abdominal) cavities were washed, with analysis of the recovered lavageate for differential cell counts and protein levels at 24 hours to assess the short-term inflammatory response and for

total foreign body giant cell (FBGC) populations at 7-days to assess chronic foreign-body-induced inflammation. After 7 days, histological quantification was also performed for granulomas (*i.e.*, scar-like lesions) on the peritoneal side of the diaphragm.

- The study authors reported evidence of asbestos-like, length-dependent, pathogenic behavior for the mice exposed to the long fiber MWCNT samples but not to the samples consisting of short or tangled fibers. The 24-hour inflammatory responses, as assessed by total PMN populations and total protein levels, and the 7-day granuloma responses were all significantly greater than controls for the two long MWCNT samples and were generally greater than those of the long-fiber amosite sample. Neither significant inflammation at 24-hours nor giant cell formation at 7-days were observed in any of the other samples lacking detectable long fibers—*i.e.*, the two curled/tangled MWCNT samples, the short-fiber amosite sample, and the nanoparticulate carbon black sample.
- Analyses for soluble metals and endotoxin contamination indicated that neither of these factors could explain the greater inflammogenicity and granuloma formation in the long fiber MWCNT samples.

#### Implications:

- While overcoming some of the major limitations and uncertainties of a prior study that reported findings suggesting asbestos-like pathogenicity of carbon nanotubes for highly elevated intraperitoneal CNT doses in a sensitive mouse strain (Takagi *et al.*, “Induction of mesothelioma in p53+/- mouse by intraperitoneal application of multi-wall carbon nanotube,” *J Toxicol Sci.* 2008 Feb;33(1):105-16), the Poland *et al.* study remains aptly titled a “pilot study” due to some notable study limitations and uncertainties. These include the use of the mesothelial lining of the body cavity of mice as a surrogate for the mesothelial lining of the chest cavity, the assumption that the observed inflammation and granuloma formation will progress to mesothelioma, and, of particular importance, the uncertainty regarding whether such a threshold dose could be achieved in the mesothelium of the pulmonary pleura for realistic inhalation exposure scenarios.
- While the findings are of toxicological significance and merit follow-up study, including longer-term inhalation studies, they are of questionable relevance to human health risk assessment. For example, it is inappropriate to directly extrapolate the findings to humans given factors such as exposure route, dose, and species differences.”
- In addition to research directed at understanding whether inhaled CNTs have a sufficient level of biopersistence to allow for migration to the pleura, research is also needed to better understand which CNTs and possibly other nanofibers/nanoparticles elicit a similar biological response. In particular, does functionalization of CNTs alter this type of toxic response? What lengths are associated with this response? What type of pulmonary dose would inhalation of CNTs yield and what fraction of deposited CNTs could migrate to the pulmonary pleura?
- These findings highlight the critical need to better understand potential human exposures to carbon nanotubes, both in the workplace and from use of consumer products. While it would appear unlikely that there would be sufficient free CNTs released during usage of a consumer product, exposure studies are needed to verify this and to quantify levels and forms of CNTs under occupational manufacturing and handling scenarios.
- Until follow-up toxicological research is conducted and there is a better understanding of potential CNT exposures, these findings support a cautious approach towards the manufacturing and handling of carbon nanotubes. Such an approach could include the development of nanomaterial-specific risk management plans, with consideration for the possible need for cautionary warnings in MSDS until additional follow-up research is available.

## Guest Contributor

### By Sam Lipson, M.S.

Director of Environmental Health, Cambridge Public Health Department

#### Development of a Municipal Health & Safety Policy for Nanomaterials

In December 2006, the city of Berkeley, California amended their hazardous materials reporting regulation to include engineered nanomaterials among those potentially harmful compounds or materials which manufacturers, processors and researchers must report to the Toxics Management Division of their Planning & Development Department. In taking this step, Berkeley effectively chose to operate under the supposition that all engineered nanoscale materials, as a scale-defined, heterogeneous chemical class, could *potentially* pose a public health concern and should be included in a code enacted to manage *recognized* hazardous materials. This regulatory action did not impose any standards or practices on how these materials should be handled, offer technical assistance to firms, or address the need for retail consumer education. It thus represented primarily a data collection mandate that was not intended to engage the sector in development of *best safety practices* for nanomaterials.

In February 2007, the Cambridge City Council recognized the significance of Berkeley’s first step toward a municipal nanomaterials policy and instructed the City Manager to review the options for regulatory oversight of engineered nanomaterials. The City Manager then forwarded this task to the Cambridge Public Health Department. In the spring of 2007, Cambridge Public Health began to identify members for a Nanomaterials Advisory Committee, which was first convened in August and met six times over the next six months. The advisory committee included individuals representing health and safety programs at MIT and Harvard, materials researchers at both universities, the nanomaterials manufacturing sector already present in the city, the Chamber of Commerce, the Museum of Science, and other professionals and Cambridge residents with appropriate training in scientific or policy disciplines.

These deliberations ranged from a review of weight-of-evidence suggesting harm from exposure to nanomaterials to more philosophical ruminations on crafting public policy without existing standards or detailed risk management norms. As the discussion progressed, partly assisted by presentations from panel members on their areas of expertise, it became clear that there was not a consensus in the group to support mandatory compliance measures at this early point in the evolution of the nanotech manufacturing and research sectors.

The committee and the department did attempt to strike the right balance in forging a recommendation on developing a municipal policy that would actually improve the prospects for greater accountability and safe practices. This required a full consideration of the public health obligation to act in the face of uncertain (and exotic) *potential* threats to workers and researchers who may be exposed to this class of materials. This assurance function was weighed against a desire to take measured steps until there was more specific evidence of possible harm from different materials and a clearer path to enforceable standards.

The recommendations forwarded to the City Manager earlier this month include a citywide inventory of nanomaterials now being used or manufactured in Cambridge, development of a site assessment team to review management of risk and share best practices, and a campaign to provide fair-minded information to retail consumers of nanomaterials. While neither Cambridge nor Berkeley had uniform industry practices or federal standards available as a baseline for oversight, both communities did take steps to address the uncertain risk associated with this exciting new field. As with the Cambridge Recombinant DNA Technology Ordinance aimed at the biotech sector (c. 1977), there is every reason to believe that reasonable public health policy will encourage our community to embrace this nano-enabled future.

## Coming In the Next Issue

New findings on the release of silver nanoparticles from commercially available sock fabrics.

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