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Editor: Barbara D. Beck, Ph.D., DABT

Dr. Beck directs Gradient's nanotechnology, toxicology, and risk assessment practices.

Associate Editor: Chris Long, Sc.D

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Recent Government Briefs

Nanotechnology: Better Guidance Is Needed to Ensure Accurate Reporting of Federal Research Focused on Environmental, Health, and Safety Risks

<http://www.gao.gov/new.items/d08402.pdf>

In March 2008, the US Government Accountability Office (GAO) was asked to evaluate the spending and research priorities of the National Nanotechnology Initiative (NNI), a comprehensive research and development program which coordinates nanotechnology-related activities in 25 federal agencies. GAO set out to determine the extent to which agencies conducted such research in the 2006 fiscal year, the agencies' and NNI's research priorities, and the effectiveness of coordinating nanotechnology research. They found that of the \$1 billion in nanotechnology research in 2006, less than \$40 million was spent studying risks associated with nanoparticles. Also, nearly 20% of the projects identified as EHS-related were not primarily related to understanding the environmental, health, and safety risks of nanotechnology. GAO recommended that better guidance be provided to agencies regarding how to report research in order to avoid labeling nanotechnology research as EHS-related when that component is not the primary focus.

OECD's Working Party on Manufactured Nanomaterials Outlines List of Nanomaterials and Endpoints for Future Study

[http://www.oecd.org/olis/2008doc.nsf/LinkTo/NT00003282/\\$FILE/JT03246895.PDF](http://www.oecd.org/olis/2008doc.nsf/LinkTo/NT00003282/$FILE/JT03246895.PDF)

On June 2, the Organisation for Economic Co-operation and Development (OECD), an intergovernmental organization of thirty countries, released its sixth report in the "Safety Of Testing Nanomaterials," series, aimed at identifying human health and environmental safety related aspects of manufactured nanomaterials. This particular report presents the completion of stage one of the project, which includes a priority list of 14 representative manufactured nanomaterials currently or expected to be used in commercial products. This list includes fullerenes, nanotubes, metal nanoparticles, carbon black, metal oxides, polystyrene, dendrimers, and metal clays. The report also lists endpoints to be studied in future hazard assessments of these nanomaterials, including endpoints related to material characterization, environmental fate, toxicology, and material safety.

Reports, Reviews, White Papers, and Books

Assuring the Safety of Nanomaterials in Food Packaging: The Regulatory Process and Key Issues

By Michael R. Taylor, Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies

http://www.nanotechproject.org/publications/archive/nano_food_packaging/

Nanomaterials have unique properties that make them potentially beneficial in food packaging; they can be used to shield foods from outside pathogens and can indicate potential product contamination. Due to the extraordinarily complex regulatory system for food packaging, questions have been raised about how nanomaterials used in food packaging are governed. The author of this report engaged in discussions with expert working groups, addressing the topics of policy, science, and industry stewardship; the author also conducted hypothetical product scenarios involving the use of nanomaterials in food packaging. The results of these exercises were used to determine if the current regulatory structure is suitable for governing the use of nanomaterials. The author found that due to stringent food packaging laws, significant data collection, scientific investment, and innovation is needed to satisfy regulations before nanomaterials can be used by the food industry. This work

needs to be done in close consultation with both the FDA and the USEPA, since both agencies play a role in regulating food packaging.

Powell, MC; Griffin, M. 2008. Bottom-Up Risk Regulation? How Nanotechnology Risk Knowledge Gaps Challenge Federal and State Environmental Agencies.

Environmental Management. Electronic publication ahead of print.

<http://www.ncbi.nlm.nih.gov/pubmed/18543023>

The authors of this paper suggest that US federal regulatory system is currently unable to adequately address potential nanotechnology risks. They suggest that under current laws and regulatory structure, nanoparticle regulation will be addressed by state- and local-level agencies in an “end-of-pipe” fashion, due to knowledge gaps and lack of federal oversight. This paper describes potential environmental risks posed by nanotechnologies, and outlines the capacities of the Toxic Substances Control Act, Clean Air Act, Clean Water Act, and Resources Conservation and Recovery Act; it explains how these current statutes can regulate potential nanotechnology risks. The paper highlights nanotechnology data gaps, and uses several environmental statutes and agencies in the state of Wisconsin as a case study of how these gaps are a problem. Last, the authors discuss advantages and disadvantages of state versus federal approaches in regulating nanotechnology. They conclude that funding should be immediately allotted to address data gaps and state that potential environmental problems from nanotechnology should be addressed in a proactive fashion, rather than be addressed after potential problems have already occurred.

Upcoming Meetings and Conferences

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.

Nano Risk Analysis: Advancing the Science for Nanomaterial Risk Management

September 10-11, Washington, DC

<http://www.srananoworkshop.org/>

Co-sponsored by the Society for Risk Analysis and the U.S. Environmental Protection Agency, this workshop will bring together experts from diverse disciplines to evaluate how the field of risk analysis can address the considerable uncertainties currently associated with impacts from nanoscale materials and nanotechnologies. It will convene experts in risk analysis, nanotechnology, environmental science, communication, and policy, as well as key stakeholders and members of the public interested in risk analysis, public health, risk communication, and nanotechnology. A mix of presentations, panels, and breakout sessions will focus on unique aspects of the risks of nanoscale materials and risk analysis for these materials. Themes will include materials characterization, exposure assessment, toxicology and dose-response assessment, uncertainty analysis, risk characterization (including risk reduction benefits of nanotechnology), and risk communication.

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

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.

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(ATSDR) 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.

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

1. Benn TM; Westerhoff, P. 2008. "Nanoparticle silver released into water from commercially available sock fabrics." *Environ. Sci. Technol.* 42(11):4133-9. Abstract: <http://pubs.acs.org/cgi-bin/abstract.cgi/esthag/2008/42/i11/abs/es7032718.html>

Synopsis:

- Nanoparticle silver (Ag_{nano}) is used to confer antimicrobial properties in consumer products such as socks, paints, bandages and food containers. In socks, Ag_{nano} is believed to inhibit the growth of odor-causing bacteria. While there may be advantages to reducing microbial growth, use and disposal of these consumer products could result in environmental release of ionic silver (Ag^+), which can be highly toxic to aquatic organisms. This study was undertaken to quantify the amount of Ag_{nano} and/or Ag^+ released from socks during washing, and to determine whether silver could be removed by municipal waste-water treatment.
- Release of silver was evaluated for six different brands of socks, from manufacturers claiming their socks contained Ag_{nano} . The amount of total silver (Ag_{nano} & Ag^+) in the different brands ranged from below the detection limit to 31 mg silver per sock. For evaluating release of Ag_{nano} during washing, socks were agitated without detergent in ultrapure water for 24 hours, four consecutive times, or three consecutive times for one hour. To evaluate the potential influence of using ultrapure water, one brand of socks was also washed using municipal water from the city of Tempe, AZ. Ag_{nano} was separated from ionic silver (Ag^+) by filtration, and a silver ion-specific electrode was used to quantify the Ag^+ . Scanning electronic microscopy (SEM) was used to confirm the presence of Ag_{nano} in the socks, and transmission electron microscopy (TEM) was used to evaluate presence of Ag_{nano} in the washwater. Adsorption of silver to biomass from a wastewater treatment plant (i.e., activated sludge) was evaluated using biomass from a bench-scale reactor as well as fresh biomass from a local wastewater treatment plant (WWTP).
- SEM confirmed the presence of Ag_{nano} in the socks. Following four consecutive 24-hour washes, the amount of total silver released from the socks ranged from below the detection limit to 1.8 mg. Two of the six brands released 100% of their silver; one released 0.5% of their silver; and for two brands the amount of Ag_{nano} released was below the detection limit. The amount of total silver released following three consecutive 24-hour washes was comparable to the amount released following three consecutive 1-hour washes (1245 vs. 1020 μg for brand #1, and 100 vs. 390 μg for brand #3), while the amount released in Tempe, AZ municipal tap water was approximately 10% of that released in ultrapure water (15 μg vs. 155 μg). Evaluation of the wash water indicated

that at least some of the silver released from the socks was in the form of Ag_{nano} , although most (approximately 70% or more) of the silver in the wash water was present as Ag^+ . Incubation of the washwater with WWTP biosolids demonstrated that WWTPs may be able to remove approximately 99.8% of influent silver, and would be able to comply with water quality criteria for fresh water and salt water at influent concentrations below 2900 and 4250 $\mu g/L$, respectively.

Implications:

- This study demonstrated that there is considerable variability in the amount of silver released from Ag_{nano} -containing socks during washing, with some socks releasing virtually all of their Ag_{nano} , and other socks not releasing any detectable silver. Thus, while some socks may retain the antimicrobial properties conferred by the Ag_{nano} , other socks may lose those properties after several washes. Given the variability in the amount of silver released from socks during washing, it would be of interest to both manufacturers and consumers to determine properties of socks as well as the manufacturing process that may influence retention or release of Ag_{nano} . From a consumer perspective, it is also of interest to note that not all socks claiming to contain Ag_{nano} did, in fact, contain detectable levels of Ag_{nano} .
- The greater retention of Ag_{nano} for the socks washed in Tempe, AZ municipal tapwater, as compared with ultrapure water, suggests that washing conditions will influence retention and release of Ag_{nano} from socks. Factors that could influence release of silver during washing include type of detergent, bleach and fabric softener; water temperature; and local water chemistry (i.e. hard vs. soft water). In addition, silver released from the socks might be able to adsorb onto other articles of clothing in the wash, which could reduce the amount of silver entering the sewer system.
- Widespread use of Ag_{nano} -containing consumer products that readily release silver could be an ecological concern. Although WWTPs may be able to remove sufficient amounts of silver such that the effluent would comply with water quality criteria, the remaining activated sludge may contain levels of silver that exceed USEPA's Toxicity Characteristic Leaching Procedure (TCLP) criterion for silver, which would limit use of biosolids as fertilizer on agricultural lands. Potential contamination with silver of biosolids used as agricultural fertilizer, and the implications of such contamination, should be evaluated and addressed before use of Ag_{nano} becomes widespread.

2. Zhang, LW; Monteiro-Riviere, NA. 2008. "Assessment of quantum dot penetration into intact, tape-stripped, abraded and flexed rat skin." *Skin Pharmacol. Physiol.* 21:166-180. Abstract: <http://content.karger.com/ProdukteDB/produkte.asp?doi=10.1159/000131080>

Synopsis:

- Quantum dots (QDs) consist of a metallic, potentially toxic cadmium/selenium core with an inorganic zinc sulfide shell and, in some cases, an organic shell. The small size and

non-quenchable fluorescent properties of QDs make them well-suited for biomedical imaging. Because workers could be exposed to QDs during the manufacture, synthesis or use of QDs, it is of interest to determine the extent to which QDs can penetrate through the skin and be absorbed into the bloodstream. Previous investigations have shown that, following intradermal injection, QDs can migrate to lymph nodes and liver, but that penetration of QDs through intact skin is minimal. This study investigated penetration of QDs through skin under conditions that may enhance dermal absorption – including flexing the skin, and tape-stripping or abrading to remove the stratum corneum, which is the major rate-limiting barrier for dermal absorption.

- Dermal absorption was evaluated for two types of QDs, both coated with carboxylic acid: QD565 – a spherical nanoparticle with a hydrodynamic diameter of 14 nm; and QD655 – an ellipsoid nanoparticle with a hydrodynamic diameter of 18 nm. Using shaved 10-week old Wistar rats, quantum dots were applied to the backs of the animals on 4 types of skin: normal skin; skin that was flexing; skin that had been tape-stripped ten times with Scotch Magic™ tape to remove the stratum corneum; and skin that had been abraded 60 times with Type 100 (3M™) sandpaper – until the skin was bright red but not bleeding, with visible blood vessels, to remove both the stratum corneum and most of the viable epidermal layers. Treated skin was then placed in two-compartment flow-through diffusion cells in which the dermal side of the skin was bathed with a flow-through physiological perfusate. Perfusate was collected hourly for eight hours, and then every four hours for the next 16 hours, to determine whether the quantum dots had penetrated through both the epidermis and dermis. Skin samples from the 8-hour and 24-hour time points were also evaluated microscopically.
- Microscopic evaluation of the skin at eight and 24 hours showed that QDs on the unperturbed skin remained attached to the hairs with some deposition on the stratum corneum, and that flexing the skin enabled the QDs to travel further down the hair shaft, also contacting the stratum corneum, but that neither of the QDs tested in this study penetrated into stratum corneum. Similarly, for the skin that had been tape-stripped to remove the stratum corneum, the quantum dots remained on the epidermis without penetration into the epidermis. On the abraded skin that lacked both the stratum corneum and the epidermis, the spherical, slightly smaller QD565 particles had penetrated approximately 70 µm into the dermis after 24 hours, with a concentration gradient from the outer to the inner layers of the dermis. In addition, some of the QD565 particles had penetrated through the outer root sheath of a hair follicle. For the slightly larger, ellipsoid QD655, there was slight penetration at both eight and 24-hours, with the particles penetrating less than 25 µm into the dermis, and much less of a concentration gradient than was observed for QD565.
- There was no fluorescence or cadmium detected in the perfusate, indicating that neither the intake QDs, nor the inner

metallic core, had penetrated completely through the dermal layer.

Implications:

- Despite their small size, dermal absorption of carboxylic-acid coated QDs after 24 hours was negligible, even for abraded skin that lacked the protective barriers of both the stratum corneum and viable epidermis. The abraded skin would be representative of skin conditions such as atopic dermatitis, psoriasis or eczema, or superficial wounds such as paper cuts, under which dermal absorption would be enhanced.
- Although the quantum dots did not completely penetrate through the viable dermis, it would be of interest to determine the ultimate fate of QDs that did penetrate into the dermis. For example, would the quantum dots remain in the dermis, or would they eventually migrate into the circulation? Also, what is the fate of the carboxylic acid and zinc sulfide shells? For example, could the shells possibly degrade, and release the core, which contains cadmium and hence could be of greater concern from a toxicological perspective?
- This study demonstrated that penetration into the dermis was somewhat greater for the smaller, spherical QDs than for the slightly larger, ellipsoid QDs, suggesting that size and shape may influence penetration. Penetration could also vary depending on the outer, organic coating. For example, the polar carboxylic acid coating may be able to bind with the hydrated keratin and thus limit penetration through the epidermal layer.
- This study also demonstrated that hair follicles may facilitate penetration of particles into the skin. However, considering that the hands are the most likely part of the body that would contact QDs during manufacture, synthesis and use; and that the hand, particularly the palmar surface, has relatively few hair follicles; absorption of QDs through hair follicles would be minimal under typical circumstances. Nonetheless, absorption of QDs through hair follicles could be a potential concern if, for example, an accidental spill resulted in exposure to the forearm, particularly if the skin damaged the skin.

Guest Contributor

By Raymond David, PhD, DABT,
BASF Corporation

Proper characterization of nanomaterials in publications – a path forward – the ‘Clancy’ score

The toxicology literature on nanomaterials is still in its infancy. We have been reared on the premise that toxicity of particles is a function of size, surface properties, and possibly other parameters. These assumptions are largely based on data from studies in which both *in vivo* and *in vitro* responses to different size particles of the same substance or of polystyrene beads coated with different organic chemicals were compared. More recently, conflicting data for these same ‘rules of thumb’ have been reported from studies in which the particles were not well characterized, so firm conclusions are difficult to make. As we now view the information in the published literature, and indeed as we conduct new studies, we are

beginning to understand that characterization of the particle in the test medium (not as described by the manufacturer or supplier) becomes critical to developing these 'rules' that we so desperately seek to reliably predict the toxicity of nanomaterials.

To aid this effort, national and international groups have developed lists of characteristics that should be measured whenever studying nanomaterials. Organizations such as OECD and ISO have proposed parameters for investigators to consider measuring (see for example the ISO TC229 guidance). Some of us in industry, academia, and government are considering hosting a workshop to get the editorial staff of appropriate journals to embrace the idea. What better driver than having characterization a 'criterion for publication'? Such a workshop is in the planning stage and is expected to take place sometime this Fall.

What do we do in the meantime? An alternative is to rate publications based on the extent of characterization – similar to the use of the 'Klimisch' score in evaluating the reliability of data on HPV chemicals - to rate the validity of characterization data on nanomaterials. Here's how the scoring might work:

0. No characterization provided. Supplier's specifications only, with no verification.
1. Nominal characterization of size. Median size of particle verified by acceptable method prior to introduction to the test system.
2. Nominal characterization of size, surface chemistry, and other relevant parameters. Median size and distribution, surface chemistry, and other relevant parameters of particle verified by acceptable methods prior to introduction to the test system.
3. Minimal data set in test system. Characterization of a limited number of parameters, such as particle size in the test medium, surface chemistry, dissolution rate, etc., verified by acceptable methods.
4. Full characterization. Characterization of all pertinent OECD parameters in the test medium verified by acceptable methods.

I call this the "Clancy" Score (after my colleague, Dr. Shaun Clancy). Perhaps as a first step, the Clancy Score will help us weigh the value of study data and pave the way toward determining criteria necessary for publication. As such, it could help guide researchers to design studies with appropriate characterization, so the results can be accurately compared from study to study.

Coming In the Next Issue

Recent research that suggests that pumpkin plants can absorb, translocate, and accumulate certain nanoparticles in the environment.

Publication Staff

Editorial

Barbara D. Beck, Ph.D., DABT
 Christopher M. Long, Sc.D.
 Noelle M. Cocoros, M.P.H.
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Production

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 Ruth Buchman
 Janelle Forbes



Contact Us

Gradient Corporation
 20 University Rd
 Cambridge, MA 02138

t: 617.395.5000
 f: 617.395.5001

email: ehsnanonews@gradientcorp.com
 website: www.gradientcorp.com

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