Nanotechnology Law Report

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New Journal on the Block. A new nanotechnology-focused publication has just announced its own launch. The Journal of Nano Education is "a peer-reviewed international journal that aims to provide the most complete and reliable source of information on current developments in nanoscale science, technology, engineering, and medical education," and is now accepting submissions for publication. In addition to publishing materials from undergraduate and graduate research, the journal will also cover topics at the K-12 levels. The Journal is targeting "various aspects of teaching and learning of nanoscale science, technology, engineering, and medicine."

The creation of another journal just shows how the field is growing. The new twist here is the coverage of all levels of nano-education. The Journal is available at http://www.aspbs.com/jne/

Nanoparticles Successfully Used in Plant Cell Delivery Study. Researchers at Iowa State University recently published the results of a study into whether nanoparticles can be used to deliver DNA into plant cells. The scientists found that porous, DNA coated, 100-200 nm diameter, silica nanoparticles entered into protoplasts (plant cells without cell walls) without causing any toxic effects. These same nanoparticles, however, would not enter into intact plant tissue cells until the particles' pores were capped with surface-functionalized gold nanoparticles. Once capped, the nanoparticles also entered into intact plant cells. The scientists theorized that the gold nanoparticle caps added extra density allowing the molecules to penetrate the intact cell walls. The scientists further concluded that these types of nanoparticles could be used to deliver into plant cells (i) DNA via their coating, and (ii) "biogenic moieties" contained inside the hollow spaces of the nanoparticles themselves. The study ended with the observation that this research is a first step in demonstrating that nanoparticles may be of use in the field of plant genomics to improve crop species.

F. Torney, et al., "Mesoporous silica nanoparticles deliver DNA and chemicals into plants," NATURE NANOTECHNOLOGY, Vol. 2, May 2007.

New Titanium Dioxide Mouse Study. Scientists at the University of Iowa exposed mice to 5 nm sized particles of titanium dioxide in order to learn about the potential health impact of manufactured nanomaterials. One group of test animals inhaled the aerosolized particles for four hours in a single day, and another group inhaled them for four hours a day for ten days. The results of the tests were encouraging. The first group of mice experienced no adverse effects. The second group "showed a significant but modest inflammatory response" that resolved itself between two and three weeks after the last exposure. The study is important because some scientists theorize titanium dioxide nanoparticles exhibit novel characteristics at sizes at or below 10 nm. Because the particles in this study fell below that size-range, the scientists were prepared for unique results – which did not occur.

The study is also noteworthy because the scientists went to great lengths to specifically characterize the nanoparticles, aerosol, exposure methods, and animals used in the experiment in great detail. It is also notable that the study purportedly used the smallest commercially available titanium nanospheres, providing a nice benchmark for future researchers.

V. Grassian, "Inhalation Exposure Study of Titanium Dioxide Nanoparticles with a Primary Particle Size of 2 to 5 nm," ENVIRONMENTAL HEALTH PERSPECTIVES, Vol. 115, No. 3 (March 2007).

NIOSH Scientists Conduct Pulmonary Exposure Study. Nine NIOSH researchers in West Virginia recently published a study regarding the potential cardiovascular effects of pulmonary exposure to SWCNTs. In the study, mice were exposed to

SWCNTs by intrapharyngeal instillation. The mice showed oxidative stress in lung, aorta, and heart tissues seven days after exposure, which decreased to control levels within 28 days. They also showed the possibility of mtDNA oxidative damage up to 60 days after exposure, and a possible increase in the risk of atherosclerosis due to exposure. The authors concluded that "[t]hese studies demonstrate that SWCNTs, under the described conditions, have the potential to influence cardiovascular diseases."

> Z. Li,. "Cardiovascular Effects of Pulmonary Exposure to Single-Wall Carbon Nanotubes," ENVIRONMENTAL HEALTH PERSPECTIVES, Vol. 115, No. 3 (March 2007).

Metal Oxide Nanoparticles: Atherosclerosis Study. Scientists from the University of California, Davis and Texas A&M recently collaborated on research into whether certain metal oxide nanoparticles may cause inflammation in the type of cells that line the human circulatory system. The authors theorized that certain types of metal oxide nanoparticles might be taken up by endothelial cells and cause endothelium inflammation, which in turn has been shown to play a central role in atherosclerosis. The scientists' in vitro experiment exposed human aortic endothelial cells to three types of metal oxide nanoparticles -- iron oxide, yttrium oxide, and zinc oxide -- under a wide range of concentrations and for exposure times ranging between 1 to 8 hours. The study found that while all three types of nanoparticles were taken up into the cells, only two caused an inflammatory response. Yttrium oxide and zinc oxide impacted inflammatory markers in the cells, while zinc oxide did not. Interestingly, the scientists believe that the size and surface area of the nanoparticles were not responsible for the amount of inflammatory response observed. The smallest nanoparticles with the largest surface area -- iron oxide -- caused no inflammatory response, while the largest particles with the smallest surface area -- zinc oxide -- caused the greatest inflammatory response in the study. The scientists cautioned that no broad conclusions should be drawn from their research, and that both in vitro testing simulating actual blood flow conditions and in vivos tests are necessary.

> A. Gojova, et al., "Induction of Inflammation in Vascular Endothelial Cells by Metal Oxide Nanoparticles: Effects of Particle Composition," ENVIRONMENTAL HEALTH PERSPECTIVES, Vol. 115, No. 3 (March 2007).

Another Critique of Berkeley's Nanomaterials Ordinance. A UC Berkeley student's recent entry into the university's Science, Technology and Engineering White Paper Competition offers another interesting perspective on the City's nanomaterials ordinance. The paper's author believes that the current open ended question format used in the City's Disclosure Guidelines is unlikely to produce data useful "in linking specific nanomaterials to the factors that cause toxicity or to adequate management and containment practices." Accordingly, the author recommends the City abandon its current question format in favor of a simpler closed question style because "laboratories are more accustomed to reporting chemicals using a closed, questionnaire style document." Beyond commenting on the format used by the City, the author also takes the position that:

> The type of information required by the ordinance fails to capture some key characteristics of nanomaterials considered to be important for the potential toxicity. Among other things, the ordinance asks for the 'average and maximum daily amount of the materials stored (in metric units), chemical form (solid, liquid), particle dimensions and approximate mass'. The ordinance does not ask for critical data on surface to mass ratio, surface coatings, or surface characteristics and reactivity potential, among other relevant factors for nano-toxicity. While the information collected by the ordinance fits well with the needs of hazardous materials business plan, the debate on how to regulate nanomaterials would benefit more from the development of a reporting form that begins to get at the key factors of nano-toxicity.

Finally, while the author questions the format and scope of the City's Disclosure Guidelines, she takes the position that the ordinance is a step in the right direction and should be used to inform other municipalities considering how to best deal with potential nano-related EHS risks.

> J. Barandiaran, "The City of Berkeley Ordinance on Nanotechnology: Steps towards a standardized nanomaterials classification framework," GOLDMAN SCHOOL OF PUBLIC POLICY, UC BERKELEY, SCIENCE TECHNOLOGY AND ENGINEERING WHITE PAPER COMPETITION, April 18, 2007.

NNI Reauthorization. The Risk Policy Report reports that Congressional re-authorization for the

National Nanotechnology Initiative, the cross-agency program designed to study nanotechnology issues, is underway. The current funding is set to expire at the end of the 2008 fiscal year.

Reports indicate that as part of the re-authorization legislation, Sen. Mark Pryor (D-AR) included an amendment to the Senate bill setting aside $40 million per year for environmental health and safety research. Aside from this fiscal directive, there are expectations that Congress will mandate the reauthorized NNI to perform more research into potential health risks associated with nanotechnology.

> **MEH**: *Re-authorization of the NNI is crucial for the advancement of our understanding of nanotechnology. Through the NNI many federal agencies can share information and research, which will serve to close the ever-present data gap that surrounds nanotechnology. At the same time, an increased call for EHS funding is not inappropriate, and it is through directed funding that specific goals can be met. While the NNI has been criticized of late, its role in the development and regulation of nanotechnology is an important one as we try and both learn about this new technology and, at the same time, begin to formulate efficient and effective regulations.*

Nano Patents: 21st Century "Sooners"? A recent Nanowerk Spotlight likens the rush to secure nanotechnology patents to the Oklahoma land rush of 1889, in which "sooners" entered the territory before the legal time of entry to claim the choice homesteads. The "sooners' in the nanotechnology patent rush are said to be those who, while not intentionally violating any rules, may have obtained unduly broad patents early and, like the "sooners" of old, find their claims subject to challenge.

Early nanotechnology patentees are more like explorers who laid claim to broad swaths of beachfront property – at low tide. None of them can be certain of the scope of the claims they will have after the tide of legal challenges rolls in. Some will find themselves still in possession of valuable beachfront property. Others will find their claims severely eroded or even swept away.

What differentiates those on the high side of the tide line from the rest? The nature of the invention, attention to the prior art, patent drafting skill, and sometimes even luck. The Spotlight focuses on inadequate disclosures in early nanotechnology patents resulting from the lack of standardized technology in a developing field, applicants seeking "windfall" claims that exceed the scope of the disclosure, and delayed nanotechnology training for patent examiners, leaving the patents vulnerable to challenge under 35 U.S.C. §112. Early – and even more recent – nanotechnology patents also may be vulnerable to challenges based on obviousness under 35 U.S.C. §103, especially in view of the U.S. Supreme Court decision in KSR v. Teleflex, No. 04–1350.

New York Academy of Sciences: Nanotoxicology Panel. In May, the New York Academy of Sciences hosted "Nanotechnology and Toxicology: Status and Strategies." The event was hosted by the Academy's Predictive Toxicology Discussion Group and was organized by the Woodrow Wilson International Center for Scholars and Gene Logic, Inc. Gunter Oberdörster from the University of Rochester gave a presentation entitled "Is Nanoparticle Toxicity Predictable?" Dr. Oberdörster began his presentation by highlighting the lack of data available to substantiate or refute potential EHS concerns related to the use of engineered nanoparticles in many applications. He noted several of the very properties of nanoparticles that make them interesting for commercial uses – small size, large surface area, ability to enter cells, translocation ability once inside the human body – might also contribute to their potential toxicity. Dr. Oberdörster went on to explain translocation, potential health effects of nanoparticles, and the hypothetical mechanisms by which such effects occur. He further argued that surface area is the proper dose metric in nanotoxicology research – not particle mass or particle number, and that exposure routes have a great deal to do with how nanoparticles translocate in the body. As an example, he pointed to a rat exposure study in which nanoparticles had two differing entry points: (i) inhalation/lung and (ii) bloodstream. The study apparently found that inhaled nanoparticles accumulated in the rats' bone marrow and liver, while nanoparticles injected into the bloodstream accumulated in the liver but not in the bone marrow. Finally, Dr. Oberdörster offer a short explanation of his work on developing a simple assay to be used in determining the toxic potential of nanoparticles.

Rounding out the panel of speakers were Andrew Maynard from the Woodrow Wilson International Center for Scholars and Wendy Sanhai from the Office of Commissioner, FDA – both of whom gave

very articulate and cogent presentations. Dr. Maynard's presentation was "Nanotechnology Science, Society and Policy," and Dr. Sanhai's presentation was "Nanotechnology: Regulatory Jurisdiction, Challenges, Future." A videotape of the event should be posted on NYAS' website later this month.

Mapping Nanotech. The Woodrow Wilson International Center for Scholar's Project on Emerging Nanotechnologies and The Pew Charitable Trusts recently created a map powered by Google Maps showing the location and types of nanotechnology appearing in the United States. The map is interactive and searchable, providing both a broad-based look at where and what kind of nanotech is developing as well as point specific operations.

First impressions show the bulk of nanotechnology located on the coasts, however, note an increased nanotech presence in the Midwest/Great Lakes region. Not surprisingly, the focus is on materials and electronics as the industries of choice.

Oh, and its fun to play with.

Natural Resources Defense Council Proposes New Nano-EHS Framework. The Natural Resources Defense Council ("NRDC") recently issued its own EHS nanotechnology framework. See J. Sass, "Nanotechnology's Invisible Threat: Small Science, Big Consequences," NRDC Issue Paper, May, 2007.

As readers may recall, NRDC is a member of the Civil Society-Labor Coalition which just last month published an open letter rejecting the DuPont Chemical Company and Environmental Defense joint voluntary "risk assessment" framework for nanotechnology. We previously expressed our disappointment with the Coalition's blanket rejection of the ED/DuPont framework without offering its own substantive comments. NRDC's issue paper provides some of the substance we felt was lacking in the Coalition's open letter. It is encouraging to see at least one Coalition member join the substantive debate rather than simply rejecting the effort out of hand.

NRDC's underlying position should be very familiar to anyone monitoring nano-EHS issues:

> "The warning bells are ringing: People are beginning to raise serious questions about the possible impact of nanomaterials on human health." . . . "In light of these threats, it is imperative that the government move quickly to establish health and safety standards for workers who manufacture these products, consumers who use them, and the environment that absorbs the waste." . . . "Governments must act preemptively to protect people form the potential dangers of nanomaterials, even though the exact health and ecological impacts are still undetermined."

While unnecessarily alarmist in tone (in our view), the general idea that government should be diligently trying to figure out how to deal with any potential nano-related EHS risk is valid, and the federal government has already made it abundantly clear that it takes these issues seriously.

A large portion of of NRDC's position, however, appears to be base on perceived inadequacies with the entire regulatory process and burdens of proof in the United States, rather than with any alleged hazard or risk specifically associated with engineered nanomaterials: "The current approach to chemical regulation is slow and costly, and it is designed to accept a level of harm as if it were a necessary cost of progress" . . . "This approach has failed for 30 years to prevent human and environmental exposures to harmful industrial chemicals."

In this same vein, NRDC argues that EPA's impending voluntary stewardship program for nanomaterials is problematic because it is voluntary. NRDC believes that "[c]ompanies with the riskiest products, as well as those with poor business ethics – that is, those most likely to need government oversight – are least likely to participate." Accordingly, NRDC argues that "a voluntary program without a mandatory regulatory component will not be able to address potential risks." Presumably, this is the same basis for the Civil Society-Labor Coalition's rejection of the ED\DuPont framework.

After explaining its basic positions on the above issues, NRDC then invokes the "precautionary principle" in crafting its own framework for regulation of commercial nanomaterials. NRDC's framework has four major components:

1. Prohibit the untested or unsafe use of nanomaterials. NRDC argues:

   "This approach must assume worst-case scenario exposure scenarios in order to prevent unsafe human exposure and releases into the environment . . ." and . . . "Such a precautionary regulatory approach places the burden on the manufacturer to provide evidence of safety prior to widespread use, rather than on regulators to prove harm."

   Obviously, this approach runs counter to current regulatory framework in the United States in several respects. It is difficult to imagine the federal government reversing many years of precedent in this regard when determining how to address potential nano-related EHS concerns.

2. Conduct full life-cycle environmental, health, and safety impact assessments as a prerequisite to commercialization. This analysis would require treating nanomaterials as new substances, and would use nanospecific toxicological testing methods. Additionally, this element of the framework would require the evaluation of company risk management practices at all points in supply chain.
3. Facilitate full and meaningful participation by the public and workers in nanotechnologies development and control; considering the social and ethical implications of nanotechnologies."

   On this point, NRDC calls for true public involvement, rather than a one way "education of the public" by government and business.

4. Finally, NRDC believes that regulatory agencies must facilitate public access to critical information by: creating a publicly available database of nanotoxicology issues; requiring labeling of all consumer products containing nanomaterials; enforcing existing "right to know" rules as they apply to nanomaterials; and creating a publicly available tracking system for all nanomaterials.

While we do not agree with many of the positions advocated by NRDC in its issue paper or the structure of its proposed framework, nonetheless it is apparent a lot of thought went into the document and that it provides some good food for thought. It is well worth reading.

Obvious Inventions: Teleflex and its Impacts. The Supreme Court's decision in KSR v. Teleflex makes it easier to show that an invention is obvious. This case is likely to result in changes in the nanotechnology field and elsewhere, including:

- For patent applicants, fewer – but perhaps more valuable – allowed patents.
- For patent owners, a greater risk to patent claims that are challenged based on obviousness.
- For patent licensees, another factor to consider when evaluating existing license agreements in view of Medimmune v. Genentech.

Here is what happened:

35 U.S.C. §103 requires that a patentable invention be nonobvious in view of the prior art. A finding of obviousness may be based on a single reference. For example, a claim for nanometer size aluminum oxide particles was found to be prima facie obvious in view of a reference that disclosed aluminum oxide particles with overlapping particle sizes and size distributions. In re Kumar, 418 F.3d 1361 (Fed. Cir. 2005). More often, though, a finding of obviousness is based on a combination of references that together disclose all elements of an invention, with elements "missing" from one reference being supplied by another reference. For example, a release agent comprising a stable emulsion of submicron size polysiloxane particles was held to be obvious in view of references that disclosed (1) a stable polysiloxane emulsion of similarly sized particles, and (2) an organopolysiloxane polymer used as a release agent. In re Ona, 38 U.S.P.Q.2d 1597 (Fed. Cir. 1995).

Before KSR, references could be combined only when there was teaching, suggestion, or motivation to combine the references at the time the invention was made (the "TSM" test). This avoided obviousness findings based on hindsight – an examiner or patent challenger could not rely on a combination of references unless the prior art pointed toward that combination. In the Ona case,

above, the first reference taught numerous uses of the microemulsion and suggested its use where stability is desired. The court noted that this teaching would motivate one of ordinary skill in the art to use the microemulsion as a release agent, as taught by the second reference.

The Supreme Court concluded that the TSM test was too rigid and could preclude fact finders from applying common sense. The Court explained that "any need or problem known in the field . . . at the time of the invention . . . can provide a reason for combining the elements in the manner claimed" and that "familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." The Court did not abolish the TSM test but opened the door to a broader range of justifications for combination of references. In addition to increasing the difficulty of obtaining new patent claims, this new standard increases the likelihood that previously allowed claims will be held invalid, particularly if an obviousness rejection was overcome during prosecution by arguing that the TSM test was not satisfied.

Colliding Worlds: Nanotech and GHGs. We here at the Nanotechnology Law Report like to think that nanotech is the "next big thing." Many think that another "next big thing" is the concern and discussion over global warming and greenhouse gases (GHGs). In May, these two big things came together in two very interesting ways.

First, the United Kingdom's Department of Food, Environment, and Rural Affairs (DEFRA), released a report entitled "Environmentally Beneficial Nanotechnologies: Barriers and Opportunities." The 95-page report outlines the opportunities nanotechnologies may provide in combating global warming through cutting the use of non-renewable energy. The report focuses on five areas: fuel additives, solar cells, hydrogen, batteries & supercapacitors, and insulation.

In a second GHG development, the Project on Emerging Nanotechnologies, of the Woodrow Wilson Center for International Scholars, has "gone green." While more details can be found at http://www.nanotechproject.org/117, the Project decided to offset its GHG emissions to zero, thereby eliminating is "carbon footprint." The Project is offsetting approximately 93 metric tons per year of carbon dioxide emissions through The Climate Trust for travel emissions and the Solar Electric Light Fund for electricity emissions. "Offsets" are those projects that have the effect of reducing the amount of greenhouse gas in the atmosphere through activities such as carbon capture, increased use of renewable energies, or increased efficiencies at existing GHG sources. The Project, therefore, is funding, through the purchase of offsets, these two organizations' efforts to reduce the amount of GHGs in the atmosphere.

While both of these developments are relatively small compared to the larger body of work on both nanotechnology and global warming, they show that the two are not necessarily distinct. We will undoubtedly see additional overlap between the two fields are more is learned concerning nanotechnology's ability to impact energy sectors.

Environmental Benefits of Nanotechnology. A recent article by Nanowerk highlights the sometimes overlooked environmental benefits that nanotechnology may provide. While much focus is placed on the environmental, health, and safety impacts that free nanomaterials may create, less mainstream discussion concerns the benefits that are being researched.

The Nanowerk article mentions programs in Europe that have the affect of monitoring or preventing pollution, such as self-cleaning paints and "anti-fouling" coatings. Further, there are at least four sites in the United States, and an at least two in Canada, using nanomaterials on an experimental basis to test groundwater remediation.

These kinds of advances in environmental protection and remediation should not be lost in the discussion over the possible impacts of nanotechnology. It is important to keep in mind that while there is potential for unintended impacts, nanotechnology can have many positive uses, including maintaining and supporting environmental health.

Nanotechnology Regulation "Urgently Needed," Says Former EPA Official. The Woodrow Wilson Center released a study entitled "EPA and Nanotechnology: Oversight for the 21st Century," authored by a former high-level EPA administrator, J. Clarence Davies. Mr. Davies argues that EPA oversight and regulation of nanotechnology is "urgently" needed.

An article in a May edition of Science Daily notes the reaction from the Wilson Center's Project on Emerging Nanotechnologies:

> *"This new report seeks to encourage EPA, Congress, and others to create an intelligent oversight approach that empowers EPA and promotes investment and innovation in new nanotechnology products and processes," said David Rejeski, director of the Project on Emerging Nanotechnologies at the Wilson Center (PEN). "As both the chair and ranking minority member of the U.S. House of Representatives Committee on Science and Technology stated last year, 'Nanotechnology is an area of research that could add billions of dollars to the U.S. economy, but that won't happen if it is shrouded in uncertainty about its [environmental, health and safety] consequences.' "*

The Science Daily article also summarizes the approach Davies recommends. Specifically, it appears Davies is focusing on creating an industry-EPA partnership to study the toxicity of nanotechnologies and creating an inter-agency coordinating group (possibly involving FDA and OSHA) to oversee nanotechnology regulation. The eventual goal, it seems, is to amend the Toxic Substances Control Act (TSCA) to expand EPA's power to regulate the area. It is promising that Davies' proposal involves significant industry cooperation in the development of any standards. One must hope that any actual regulations or amendments to the TSCA that come from this type of approach are properly balanced to encourage innovation and America's entrepreneurial spirit.

Events and Publications

NanoBio 2007. John Monica is speaking on nanobiotechnology and medicine product liability issues at the 2nd International Congress on NanoBiotechnology & Nanomedicine taking place in San Francisco, California from June 18-21, 2007. John will also be teaching a nanoproduct liability workshop at the Congress.

Nanomaterials Symposium. John Monica is speaking on "Possible Adverse Consequences of Premature Nanotechnology Regulation" at Intertech-Pira's upcoming 3 day nanomaterials workshop and symposium taking place in Denver, Colorado from June 25 - 27, 2007.

Nanotechnology Symposium. John Monica is speaking on "EPA regulation of nanotechnology" at the World Future Society's upcoming "Nanotechnology: Innovations and Opportunities" symposium taking place in Minneapolis, Minnesota on July 29, 2007.

Nanocomposites 2007. John Monica is speaking on "Government Regulation of Nanotechnology" at ECM's upcoming 3 day polymeric nanocomposite symposium taking place in Las Vegas, Nevada from September 5 - 7, 2007.

Nanotechnology Application Summit. Porter Wright's nanotechnology practice group will be teaching an Environmental Health and Safety workshop at NanoAppSummit 2007 taking place in Cleveland, Ohio on October 22 - 25, 2007. The group is also taking an active role in assisting with the summit and in arranging speakers. The summit will offer four days of interesting activities including: a basic nanotechnology tutorial; EHS workshop; automotive session; cleantech session; and defense application session.

New EPA White Paper Article in Small Times. John Monica and Michael Heintz have just published a short article regarding the white paper for publication in the print edition of Small Times Magazine.

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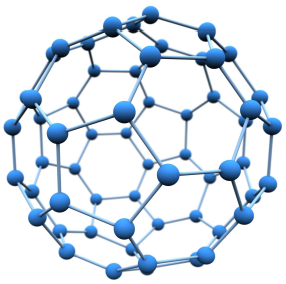

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