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Nanotechnologies: The Promise and the Peril

*by Jennifer Sass, Patrice Simms, and Elliott Negin**

Introduction

Despite the incredible potential of engineered nanomaterials to advance cleaner, safer technology, emerging data continue to indicate serious potential for harm to human health and ecological systems. Nanoscale materials, engineered to be one to one hundred nanometers ("nm"), currently have a number of commercial applications, from high-capacity computer drives to food packaging, shampoos, sunscreens, and cosmetics. The word "nanos," from the Greek word for "dwarf," indicates 10^{-9}, or one-billionth. Nanometer-sized materials are one-billionth of a meter in size; larger than atoms, but much smaller than a cell. As a comparison, there are as many nanometers in an inch as there are inches in four hundred miles (25,344,000). The width of a human hair is 80,000 nm.

Scientists predict that these submicroscopic nanoparticles, or ultra-fine particles, will give rise to new cancer therapies, pollution-neutralizing compounds, more durable consumer products, advanced detectors for such biohazards as anthrax, and higher-efficiency fuel cells, among other things. These predictions are due to the unique properties of nanoscale materials compared with their normal-size counterparts.[1] However, laboratory studies already warn that nanoparticles can cause inflammation, damage brain cells, and cause pre-cancerous lesions. Early research also has found that nanoparticles easily pass through body tissues from one area of the body to another. Responsible regulation and oversight will be needed to prevent harmful exposures.

Beyond some basic experimental data on cells and in animals, there is very little known about the toxicity of nanomaterials.

Beyond some basic experimental data on cells and in animals, there is very little known about the toxicity of nanomaterials. For example, we know nothing about whether nanomaterials in products such as cosmetics and shampoos penetrate the skin, or vaporize or off-gas from consumer products. When considering the potential for harmful effects from nanomaterials, there are two lines of evidence that are helpful: first, what is known from well-conducted scientific tests published in the peer-reviewed journals; and second, what can be extrapolated from the substantial data on the harmful effects of ultrafine particulate air pollution.

Small Size, Big Risks

Carbon-based nanomaterials, such as miniscule carbon cylinders called nanotubes and tiny carbon spheres called buckyballs, have desirable electrical, mechanical, and thermal properties, useful for such applications as developing strong, lightweight building and packing materials, computers, and aerospace engineering. However, the data thus far indicate that exposure to various carbon nanomaterials may be harmful to the brain, lung, cardiovascular, and immune systems. Carbon nanotubes tend to cluster into "ropes," acting more like fibers than particles when inhaled, giving rise to lung inflammation and granulomas (clusters of cells with injury or inflammation) that may form scar tissue (fibrosis). Nanotubes are also insoluble and cannot be broken down by the body's natural processes.

Single-walled carbon nanotubes ("SWCNTs") have been reported by five different research groups to be associated with lung toxicity.[2] Government researchers from the National Institute of Occupational Safety and Health ("NIOSH") reported rapid lung inflammation, rapid progressive fibrosis, and granulomas within seven days after a single dose of SWCNTs into the lungs of mice.[3] Cell damage increased in a dose-dependent manner by one day after exposure. One year earlier, DuPont researchers had reported acute lung toxicity and transient inflammation in rats associated with a single dose of SWCNTs of either 1 or 5 mg/kg administered into the upper lung.[4] That same year, a collaboration between the National Air and Space Administration ("NASA") and the University of Texas reported dose-dependent granulomas and inflammation in mice that were administered a single dose of either 0.1 or 0.5 mg of single-walled carbon nanotubes into the lungs, roughly equivalent to a mouse inhaling nanotubes for about three and a half workdays (low dose) or seventeen workdays (high dose) at the workplace standard for graphite dust. [5]

Despite these data, and the lack of complete safety testing, a major supplier of carbon nanotubes, Carbon Nanotechnologies, Inc., has registered its product under the Toxic Substances Control Act ("TSCA") as a synthetic graphite. Workplace haz-

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ard labels or material safety data sheets reference the workplace permissible exposure limits for graphite (15 mg/m^3 of total dust, and 5 mg/m^3 for the breathable fraction).[6] Scientists have warned that workers breathing nanotube dust at a fraction of the workplace allowable level "would likely develop serious lung lesions."[7]

Nanomaterials can also be composed of metal atoms. Examples include nanogold, nanosilver, silicon nanowires, reactive metal oxides such as nanotitanium dioxide, and quantum dots – a closely packed semiconductor crystal with unique optical and light-emitting properties. Evidence suggests that metal-based nanomaterials can cause damage to humans and the environment. In 2005, researchers from the New Jersey Institute of Technology reported that the root growth of corn, cucumbers, cabbage, carrots, and soybeans was stunted after a 24-hour exposure to high doses (2 mg/mL) of alumina nanoparticles in water.[8] Alumina nanoparticles currently are used in scratch- and abrasion-resistant coatings on commercial products such as safety glasses, car finishes, and flooring. Researchers from the University of California at San Diego reported that cadmium-selenium core semiconductor (quantum) dots used in biological imaging were acutely toxic to liver cells in a Petri dish at doses typically used for imaging.[9] The dots are replacing traditional imaging with fluorescent dyes, due to their enhanced and longer-lasting brightness.

University of Rochester investigators reported in 2000 that nano-teflon fumes (about 16 nm) were much more acutely toxic than Teflon, the popular brand name for polytetrafluoroethylene, when inhaled for only fifteen minutes by rodents, and rapidly passed through epithelial tissues to other parts of the body, inducing severe inflammation, edema, and hemorrhage of lungs within hours after exposure.[10] In 1992, University of Rochester investigators examined the effects of exposure to nano titanium dioxide (TiO_2; 20 nm), a material in sunscreen. The study showed that rodents that inhaled ultra-fine TiO_2 for three months, under conditions simulating occupational exposures (six hours/day, five days/week), had significantly more lung inflammation and scar tissue compared with those that inhaled larger TiO_2 particles (250 nm).[11]

Heeding the Red Flags

Although there is a paucity of toxicity data on nanomaterials *per se*, the hazards of nano-sized (ultra-fine) air pollution are well-documented. Particulate matter less than 10 micrometers (PM_{10}; 10,000 nm) is linked to increased disease and death from lung cancer and cardiopulmonary disease.[12] These diseases are more closely linked with exposure to smaller particles than to larger-sized ones.[13] The risks are especially high among sensitive individuals, such as those with pre-existing conditions of the heart and lungs, including asthma and chronic obstructive pulmonary disease.[14]

Some of the acute toxicity of ultra-fine particles is likely due to their larger surface-area–to-mass ratio, ability to penetrate biological tissues, and their increased biopersistance compared with larger particles of the same composition.[15] Given these characteristics and the results of targeted studies such as those mentioned above, the potential for harmful effects from widespread use of nanomaterials must be taken seriously.

Misallocation of Federal Spending

Despite these early warnings, government response thus far to the potential risks has been woefully inadequate. In spring 2005, the President's Council of Advisors on Science and Technology issued its five year review of the interagency National Nanotechnology Initiative, established in 1991 to direct federal research activities on nanotechnology.[16] Although the text of the report is 46 pages long, the section addressing "Environmental, Health and Safety" does not appear until page 35 and is less than one page long. According to the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars, only four percent of the fiscal year ("FY") 2006 federal nanotechnology funding was earmarked for research on health and environmental effects, and another four percent on social implications and education.[17] Meanwhile, federal funding for nanotechnology research and development has soared from $464 million in 2001 to $1.2 billion in FY 2007.[18] Of this investment, the National Science Foundation will get $373 million. More than $600 million is earmarked for the U.S. Departments of Defense ($345 million) and Energy ($258 million). By comparison, only $142 million is slated for the human health and environment protection branches of the federal government, the U.S. Environmental Protection Agency ("EPA") ($9 million), and the U.S. Department of Health and Human Services ($133 million), which includes the National Institutes of Health. With this disparity in funding priorities, it is hard to imagine how safety testing could ever catch up with research and development.

Some federal agencies are addressing the potential downside of nanotechnology. The Department of Health and Human Services' National Toxicology Program is researching potential health risks. In addition, NIOSH is developing a "best practices" document on handling nanoparticles in the workplace to reduce risks. In FY 2005 the EPA awarded $4 million for research on nanotechnology impacts on human health and the environment. However, much more needs to be done to better understand the potential risks of nanotechnologies.

Response by Industry and its Financiers

The private sector response to potential health and environment threats has been mixed. Some corporations seem concerned only about public perception and hope to disavow actual risk by avoiding safety testing, keeping safety data confidential, and providing empty reassurances to the public. Fearing actual or perceived risks, insurance companies such as Swiss Re,[19] and financial investment advisers such as Innovest[20] and Allianz,[21] have called for safety testing and regulatory oversight of nanomaterials. Other large corporations and many small start-up companies also would welcome safety testing and regulations if they were not overly costly or burdensome, because they would contribute to market stability by reducing future risks of liabilities and consumer rejection.

Regulatory Blind Spot

Unfortunately, existing environmental laws render federal agencies ill-equipped to regulate the nanotech industry.[22] TSCA, enacted by Congress in 1976 to gather information about chemical substances and control those deemed dangerous to the public or the environment, is the most obvious candidate for regulating nanomaterials. But TSCA lacks an effective means of requiring companies to provide risk data, and it places the burden on the government to demonstrate unacceptable risk before it can adopt regulatory restrictions of any kind.

In response to a proposal by the EPA for a voluntary program to "regulate" nanomaterials,[23] in June 2005, Natural Resources Defense Council ("NRDC") and other public interest groups urged the EPA to identify all engineered nanomaterials as "new chemical substances" under TSCA because they meet the standard of "organic or inorganic substance[s] of a particular molecular identity."[24] This would trigger TSCA section 5 pre-manufacture notice ("PMN") reporting requirements prior to the commercial manufacture or import of nanomaterials.[25] The U.S. Patent and Trademark Office issued more than 8,600 nanotechnology-related patents in 2003,[26] suggesting that at least one arm of the government already considers these materials to be new.

Existing environmental laws render federal agencies essentially impotent to regulate the nanotech industry.

In addition to PMN reporting, the 2005 NRDC comments urged the EPA to issue test rules under TSCA's section 4 by waiving the regulatory production volume thresholds that otherwise would not be triggered by the miniscule product volume of nanomaterials.[27] The groups also called for regulations under TSCA's section 6, requiring the EPA to prohibit or limit anyone manufacturing, importing, processing, distributing in commerce, using, or disposing of a chemical if there is a reasonable basis to conclude the chemical presents, or will present, an "unreasonable risk of injury to health or the environment." Tragically, the EPA has failed to regulate any new chemical using the TSCA's section 6 authority since that provision was gutted by the U.S. Court of Appeals for the Fifth Circuit in the 1991 case *Corrosion Proof Fittings v. EPA* (rejecting the EPA's application of the TSCA's section six to asbestos).[28] The court's decision and subsequent problematic EPA interpretations of that decision make it extraordinarily difficult for the agency to adopt regulations under section 6 of TSCA. Thus, NRDC stated that "while requiring [pre-manufacture notice], issuing test rules, and promulgating regulations under TSCA are necessary steps for nanomaterials, such actions will be insufficient to protect public health and the environment. Ultimately, additional legislative action by Congress, the states, and potentially the courts will be necessary to ensure that nanomaterials are adequately addressed."[29]

Other laws also are inadequate. For example, the Food, Drug, and Cosmetic Act ("FDCA") leaves all cosmetics essentially unregulated, and the chronically under-enforced Occupational Safety and Health Act ("OSHA") does not adequately protect worker health. Thus, neither the FDCA nor the OSHA is viable as a vehicle for protecting the public. Other environmental statutes are similarly ill-equipped to address nanomaterials – for example, these materials would be effectively unregulated under the Clean Air Act due to very small production quantities.

Voluntary Safety Testing is Not Enough

In response to the lack of a regulatory framework for nanotechnology, the EPA is developing a voluntary program that will ask nanomaterial producers to submit basic information on material characterization, toxicity, exposure potential, and risk management practices. A company would then be able to advertise its participation as a means of dispelling public fears about its product. A more in-depth level of participation would generate more detailed risk information. NRDC participated in an ad-hoc working group with industry, academic, and public interest groups to advise the EPA on a general framework for such a program.

While this program potentially would fill a gap in the absence of real regulations, it is severely limited in several important ways. Participation is not mandatory, and would only include those products that participating companies choose to disclose. Those companies with the riskiest products, as well as those with poor business ethics, are unlikely to participate. The program also lacks punitive measures; it will do little more than gather data – primarily industry-generated data, which experience has shown are less likely than data from the government or independent studies to report products' harmful effects.[30] In the past, industries have gone to great lengths to downplay the health risks of asbestos, lead, vinyl chloride, and other toxic materials, only to have them lead to devastating occupational and public health consequences.

EPA's White Paper Recommendations

In December 2005 the EPA issued the "External Draft Nanotechnology White Paper"[31] which made the following reasonable suggestions as first steps forward:

- Support approaches to promote pollution prevention, sustainable resource use, and good product stewardship in the production and use of nanomaterials;
- Support and undertake research on human health and ecological impacts of nanomaterials;
- Conduct case studies on the risks and information gaps of specific nanomaterials;
- Expand collaborations on the potential human and environmental health implications;
- Convene a standing cross-agency group to share risk

information and regulatory activities; and

- Expand efforts to train agency scientists and managers about the potential environmental applications and implications of nanotechnologies.

Public Interest Group Responses

An array of good stewardship approaches to nanotechnology development would increase public confidence and market stability. In NRDC comments to the EPA, signed by twenty other public interest groups, including Greenpeace International, the Sierra Club, Friends of the Earth, Environmental Working Group, ETC group, and Silicon Valley Toxics Coalition, the organizations insisted that the federal government take action on the following initiatives:[32]

- Prevent uses of nanomaterials that may result in human exposures or environmental releases unless reasonable assurances of safety are demonstrated beforehand;
- Label products that contain nanomaterials or are made with processes that use nanomaterials;
- Publicly disclose information on potential risks;
- Include toxicity information about nanomaterials on workplace hazard labels;
- Increase safety testing conducted by independent or government laboratories subject to "sunshine laws" that allow public access to information; and
- Conduct comprehensive assessment of the environmental and human health concerns that may arise across the life-cycle – including production, use, and disposal – of nanotech products.

Conclusion

While we know enough to want to avoid exposure to nanomaterials and releases into the environment, many issues need to be further studied. For example, we do not know much about how these materials harm our health over a lifetime of exposure; long-term effects have not been studied in experimental animal tests. While ingestion and skin penetration are potential routes of exposure, most studies have only tried to mimic inhalation. The majority of toxicological studies with nanomaterials have been *in vitro* (such as skin cell toxicity), or short-term animal studies. We do not know whether these materials penetrate through our skin, even though consumers use shampoos, cosmetics, and other household products with nanomaterial ingredients. We do not know if nanomaterials are aerosolized and then inhaled when we use shampoos with nano-ingredients. We do not know whether ingestion results in toxicity, although we have nanomaterials in food packaging and even in chocolate chewing gum. We know that toxicity of inhaled particles seems to increase as the particle size becomes smaller, but we lack efficient and cost-effective ways to measure the size distribution of airborne particles.

Many other questions remain unanswered. For example, we do not know the extent to which nanomaterials can penetrate the placenta and transfer from mother to baby. In addition, we are unaware whether nanomaterials are released from products when they are incinerated, buried, or degraded over time. These uncertainties indicate that a necessary first step to effective nanotechnology regulation will require investing in studies to evaluate the risks, as well as the benefits, of nanomaterials on human health and the environment.

Endnotes: Nanotechnologies: The Promise and the Peril

[1] At nano-size, opaque materials may become transparent, chemically stable materials may become reactive, and electrical insulators may become conductors, or vice-versa.

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[3] Shvedova, *supra* note 2. (This study tested occupationally relevant exposure levels: 0-40 mg per mouse administered deep into the throat, based on the workplace limit for graphite (carbon) particles (a twenty mg dose in a mouse is roughly equivalent to twenty workdays of human exposure at the workplace permissible exposure limit for graphite)).

[4] Warheit, *supra* note 2.

[5] Lam, *supra,* note 2.

[6] The National Institute for Occupational Safety and Health ("NIOSH"), 1988 OSHA PEL Project Documentation: List by Chemical Name - Graphite, Synthetic: card number 0406 (1988), *available at* http://www.cdc.gov/niosh/pel88/npelname.html (last visited Mar. 12, 2006).

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[10] Chris Johnston et al., *Pulmonary Effects Induced by Ultrafine PTFE Particles*, 168 Toxicol. Appl. Pharmacol. 208-215 (2000).

[11] *See* Gunter Oberdorster et al., *Role of the Alveolar Macrophage in Lung Injury: Studies With Ultrafine Particles*, 97 Env't Health Perspect. 193-99 (Jul. 1997); *see also* Raymond B. Baggs et al.,

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24 Toxic Substances Control Act ("TSCA") § 3(2)(A); 42 U.S.C. § 2602(2)(A).

25 *See* TSCA, *id.*, at § 5 (authorizing the EPA to review activities associated with the manufacture, processing, use, distribution in commerce, and disposal of any new chemical substance before it enters commerce, and requiring pre-manufacture notice ("PMN") reporting prior to commercial manufacture or import under § 5 and 42 U.S.C. §2604).

26 PCAST, *supra* note 16.

27 *See* TSCA, *supra* note 24, at § 4(a) (stating that where there are insufficient data to assess the effects of the manufacture, distribution, processing, use or disposal of a chemical substance, and testing is necessary to develop such data, the TSCA provides that the EPA shall promulgate regulations requiring manufacturers and/or processors of such substances to develop new data that are needed to assess potential risks to human health and the environmental if the administrator finds: (1) that manufacture, distribution, use, and disposal practices may present an unreasonable risk of injury (§ 4(a)(1)(A)(i)); or (2) that the chemical will be produced in substantial quantities and that it enters or may be reasonably anticipated to enter the environment in substantial quantities or that there is or may be significant or substantial human exposure to the substance, § 4(a)(1)(B)(i)).

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