

Baby Steps

By Umair Abdul

If you were to believe science fiction lore, nanotechnology is the stuff of nightmares. Take the recent film I, Robot, where "nanites" were depicted as tiny nanorobots designed to erase memories. Or what about the world in Michael Crichton's 1992 novel, Prey, where nanotechnology played the most villainous of villains?

In the real world, nanotechnology has revealed a new realm of possibility for scientific research, the fruits of which may vastly improve overall quality of life. Case in point: nanoresearch, the scientific art of manipulating matter at the nanoscale, has

shown how microscopic rods called carbon nanotubes can be used to kill cancer cells.

"Nanotechnology is the industry of the future," suggests Dr. Nils Petersen, director of the National Institute of Nanotechnology (NINT) in Edmonton. "The medical revolution started about 500 years ago, when we started working on the micro-scale level. Working on smaller scales is something we are just starting to understand better now," Dr. Petersen says.

People wanting to see nanotechnology up close don't need access to a state-of-the-art research facility. A simple trek to the local



department store would suffice.

Nanoparticles are used in hundreds of consumer products, from cosmetics to cleaning supplies and electronics. In fact, the average person's first brush with nanotechnology may have come with the application of sunscreen, the nanosized particles of titanium oxide and zinc oxide offering excellent protection against the sun's harmful rays.

Over the next five to 25 years, Dr. Petersen expects that nanotechnology will have a transformational impact on the way we live, ushering in new products, new

ways of sensing the world, and all kinds of new tools.

But as researchers work toward developing nanoscale solutions, bigger questions remain about nanotechnology's implications. While these may pale in comparison with the sinister monsters paraded by the sci-fi genre, they may be of crucial importance to occupational health and safety. What effect can nanomaterials have on human health? What measures and equipment will be needed to protect workers? Will existing protocols be useable in this emerging sector?

PICTURES BY ANASTASIOS JOHN HART

Wake-up call

In 2006, an aerosol-based household glass and ceramic tile sealant called "Magic Nano" came under fire in Germany when users began reporting mild to severe respiratory symptoms. News of the bathroom cleaner's health effects captured international headlines, and almost 100 people reported problems. Additionally, six people were hospitalized because of water in the lungs, or pulmonary edema.

Ironically, the German Federal Institute for Risk Assessment later released a prepared statement noting that nanoparticles were actually not part of the product mix.

However, for the nanotechnology industry, the "Magic Nano" debacle may serve as a wake-up call. First, it draws attention to the fact that some nanomaterials have been brought to market despite a lack of information concerning their effects on human health. Second, it highlights the need for public information about the potential risks and anticipated benefits of nanotechnology.

A clear understanding — whether that of the public, regulators or workplace parties — is essential given that nanoscale research and emerging nanomaterials have gained a footing in many applications and sectors.

Not much, not enough

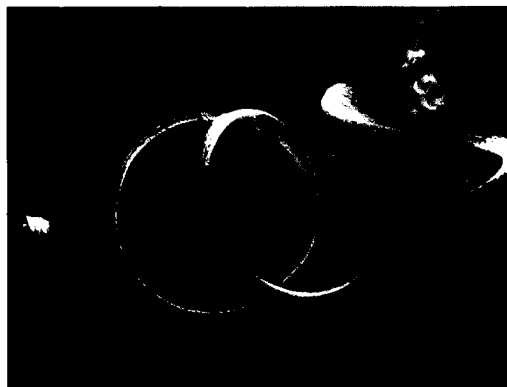
Researchers report that working at the nanoscale allows the properties of a material to be changed by increasing its surface area. Nanoparticles, for example, have increased reactivity because of the greater number of atoms at the surface.

Dr. Petersen explains it this way: A person is unlikely to get very far by trying to extract coffee from a coffee bean. Grinding the bean into smaller particles promises to reap better results.

While all this may hold promise for the future, what's known — right now — about the effect of nanomaterials on human health? So say many researchers: not much, and not enough.

Experts in the field, in general, suggest that more needs to be known before drawing broad-based conclusions. "It's unclear right now whether nanomaterials are going to pose any new risks, but, in part, that's because we don't have the ability to make definitive studies," suggests Jo Anne Shatkin, author of *Nanotechnology: Health and Environmental Risks*.

Certainly, nanotoxicology studies have been completed, some



yielding rather alarming results. Most recently, a study published in *Nature Nanotechnology* earlier this year suggested that carbon nanotubes, those rods on the nanoscale, have some unwelcome similarities with asbestos.

Headed by professor Kenneth Donaldson of the University of Edinburgh, researchers injected material into the abdominal cavities of mice. The scientists concluded that long and thin nanotubes had the same effects as long, thin asbestos fibres.

Citing similar conclusions reached by researchers from the United Kingdom in 2004, the Friends of the Earth note in a release that "to avoid a repeat of the asbestos tragedy," there should be an immediate moratorium on the commercial use of carbon nanotubes and the sale of products that incorporate nanotubes. And this moratorium should remain in place, members of the Australian group argued, until the following had been completed:

- research can demonstrate whether or not there is any safe level of exposure to nanotubes;
- new nanotechnology-specific regulation is introduced to protect the health of workers, the public and the environment;
- all nanomaterials used in work-

place settings and in consumer products are subject to mandatory labelling; and,

- the public is given a meaningful role in decision-making about nanotechnology governance, policy development and research priorities.

The comparison to asbestos is particularly resonant with health and safety practitioners, what with the crushing experience of mesothelioma, asbestosis and lung cancer.

Several toxicity studies have also been conducted on fullerenes, spherical cages that contain anywhere from 28 to 100-plus carbon atoms, says a recently released report by the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), a scientific research group in Montreal. Toxic effects have been reported after ingestion and injection in rats, the review notes.

And just this past August, researchers from the University of Michigan (U-M), through a simulation, concluded that the carbon nanoparticles released by diesel engines can get trapped in the lungs and inhibit the function of a fluid that facilitates breathing.

"Computer simulations indicated [carbon nanoparticles] wouldn't be expelled, but would become trapped in the surfactant,

entangled with fatty lipid molecules that wrapped their tails around the nanoparticles and into their central cavities," says a statement from U-M. Other studies have shown that build-up of nanoparticles in the lungs can lead to inflammation, blood clotting and changes in breathing and heart rates, the statement adds.

"There is mounting evidence that very small particles have a greater negative impact on health than larger particles," notes Angela Violi, assistant professor in the College of Engineering at U-M.

Still, researchers in general are loathe to definitively state which nanomaterials may be dangerous to human health, and which ones may not be. With each material the subject of only a handful of studies, views of the results are oftentimes divisive.

"A lot of people are doing studies, and I want to really emphasize that it's hard to compare different studies by different researchers," Shatkin cautions.

The IRSST recently released two reports. One of them, "Health Effects of Nanoparticles," concludes that understanding of toxic effects is "relatively limited," but points out that available data indicates nanoparticles can pass through different protective barriers, and be distributed throughout the body.

"Toxic effects have already been documented at the pulmonary, cardiac, reproductive, renal, cutaneous and cellular levels, while nanoparticles can be distributed throughout the body, including the interior of cells," the IRSST report states. "Significant accumulations have been shown in the lungs, brain, liver, spleen and bones," the findings add.

Business venture

To the undiscerning eye, the research samples that Shane Journey used to work with look like table salt, a small quantity of white powder in a tube. As a PhD student at the University of Saskatchewan in Saskatoon, Journey first became interested in the toxicity of nanomaterials in late 2003, when the first nanotoxicology studies emerged.

A background in occupational health, with a focus on industrial ergonomics, helped shape his view of the future potential of nanomaterials. Journey studied rosette nanotubes, an organic and water-soluble material developed in Edmonton, by injecting them into the lungs of mice.

Since his entry into the field, Journey has seen nanotoxicology grow from "probably only two or three true engineered nanomaterial toxicity studies" to a legitimate research area. "One thing I have been able to experience is watching the science evolve," he says.

"Nanotechnology is going to be ubiquitous. I have no doubt that it's going to bring widespread impact," Journey contends.

And the pursuit of all things nano seems not to be abating any

time soon. In recent years, governments and large corporations have sunk a lot of money into nanotechnology research and development, hoping to carve out territory in an expanding sector. Some industry estimates foresee nanotechnology as an annual world market of \$1 trillion by 2015, the IRSST reports.

"Nano is not just a technology. It's a suite of converging appli-



cations that are bringing them together," explains Dr. Michael Mehta, a professor of sociology at the University of Alberta in Edmonton, and one of the first researchers to shine light on the regulatory issues of entering the nanoeconomy.

The evolution of the nanotechnology business, however, may be on a collision course with consumer and occupational health and safety. Nanotechnology research spending dwarves the amount of research being done into possible health effects.

For instance, the Washington, DC-based Project on Emerging Nanotechnologies (PEN) assessed 2006 funding and found that European nations spend almost twice as much on nano risk research as the United States. Specifically, PEN found the U.S. spent \$13 million on such projects, while Europe's total was \$24 million.

PEN concluded that less than three per cent of the US\$1.4-billion federal nanotechnology research budget was being spent on environment, health and safety research.

"There is very little research being sponsored on the biological effects and how they react with the environment, and it's those sorts of properties that we need to understand in order to be able to do a quantitative risk assessment," says Pekka Sinervo, former dean of the University of Toronto's Faculty of Arts and Science, and chair of an expert panel established by the Council of Canadian Academies to answer the federal health minister's questions about the regulatory challenges associated with nanomaterials.

Moving forward, securing appropriate funding for nanotoxicology projects may prove an obstacle, especially given the complexity of the subject materials. For instance, Marc Baril, a researcher with the IRSST, notes that for a single inhalation toxicology study on a nanoparticle, researchers must look at as many as four or five different parameters. "You are talking about millions and millions of dollars, just to study one substance," Baril goes on to explain.

Measure for measure

Trying to get a handle on the characteristics leading to toxicity has proved a challenge. "The properties of nanoparticles are so many — we have got size, surface area, coating, solubility, charge," says Journey. "All of these things can affect their toxicity, and require greater controls in the studies," he says.

"Our usual way of measuring doses, which is on a basis of mass, is really turning out not to be an appropriate measure," says Shatkin. And because of their relative small size and larger surface area, she and others point out that nanoparticles in small quantities could still have major toxic effects.

The Canadian expert panel concluded that without systematic and standardized classification and measuring equipment, researchers will be presented with significant difficulties in monitoring nanomaterial exposure in both the workplace and the environment. "We simply don't have the tools that have the sensitivity," Sinervo suggests. "These are extraordinarily small particles, typically a hundred times smaller than the micro-sized particles we have given priority to."

Information from the IRSST indicates the principal way that nanoparticles are absorbed in an occupational setting is the respiratory route. Traditional protection should be effective against nanomaterials, the agency notes, but that remains to be proven.

It's also not clear how cutaneous exposure may influence health down the road. Some experts have suggested double gloving just in case.

Toronto-based Northern Nanotechnologies develops and supplies custom nanomaterials to both industry and researchers. The company performs swipe tests and, when personnel do work with nanomaterials, the process is usually done in solution. "As long as [the materials] are not agitated, there is no worry about aerosolization," contends Keith Thomas, president of Northern Nanotechnologies. "It seems to be that the big concern really is airborne particulate."

Many industry players agree there must be a higher priority on research into metrology and effective monitoring and surveillance strategies.



The Nanoscience and Nanotechnology Institute at the University of Iowa is trying to narrow things to a manageable field. Established in 2006, the institute has adopted an integrated approach to its study focus: issues related to the implications of nanoscience and nanotechnology.

"We would like to fully integrate studies of the physical and chemical properties of commercially manufactured nanoparticles with inhalation toxicological studies of the same nanoparticles, to determine those properties that most significantly affect nanoparticle toxicity," explains group director, professor Vicki Grassian.

Additionally, when working with nanoparticles, a need exists for new standards and the development of standardized measuring equipment. Traditional methods of risk evaluation, which are often based on the chemical composition and the mass of the product, sources report, are ineffective when dealing with nanomaterials.

A small effort

Health and safety practitioners trying to limit the exposure to potentially harmful nanomaterials on the job are left with questions and gaps in research. Nanotoxicological researchers suggest that the oh&s community err on the side of caution and proceed with care.

Following the risk assessment and analysis model, Shatkin recommends assessing where exposures may occur and designing those exposures out of the process. Because nanomanufacturing is relatively new, one benefit is that employers can choose to design closed systems, without having to dismantle existing structures and approaches.

When developing its workplace policy, Thomas says officials at Northern Nanotechnologies approach the problem by assuming the worst. "We are in this for the long game, not for the short

game," he says. "If you have an impact on your employees, it's going to come back and bite you."

There is some movement on disseminating safe-handling information to employers and occupational health specialists. The IRSST, along with the Commission de la santé et de la sécurité du travail (CSST) and Nano Quebec, expect to release a "best practices" guide later this year, offering current information on how best to limit exposure.

Outside of Canada, the International Council on Nanotechnology is developing a "wiki" site to address occupational safe-handling practices.

Input all around

Dr. Mehta, who has spent much of his time exploring the relationship between science and society, says he sees significant similarities between the emerging field of nanotechnology and both nuclear power and biotechnology.

Studying nuclear power safety issues before moving on to genetically modified foods, "what was striking about the links between the [two fields] was that there were a huge number of parallels," he says. "There were large regulatory gaps, there were oh&s issues, and also there were debates that were fermenting around the world, but not necessarily getting public attention."

In a recent paper, Dr. Mehta noted the "triple helix" of state, university and industry is missing the crucial fourth helix: the public. As thoughts turn to regulating nanotechnology, he advises that the public must play a crucial role early in the process to avoid the missteps made in regulating biotechnology.

"The public should have a deciding vote, because the public is the recipient of benefits and risks," Dr. Mehta argues. "It jeopardizes the potential of emerging technologies, with good science, but bad politics," he adds.

The idea of integrating public opinion in regulatory decisions has been echoed by many in the nanotechnology community. The Canadian panel — in its report, "Small is Different: A Science Perspective on the Regulatory Challenges of the Nanoscale" — noted that nanotechnology's future development is somewhat dependent

on the public's reception. "One of the elements of a successful regulatory approach is adequate regulatory consultation with the people who actually take responsibility for what's a tolerable risk, and what's not," says panel chair Sinervo.

But where do workers stand? These are the people who will take on responsibility for the risks associated with nanoparticles as they are commercialized. "The workers should be our first pri-

orities because, in many ways, they are the sentinel indicators of the potential risks," suggests Dr. Mehta.

At this time, workers here don't have much to go on when dealing with nanomaterials. (There is no nanomaterial-specific regulation anywhere in Canada, although both Health Canada and Environment Canada are taking the first steps to gain a clear understanding of the unique characteristics of nanoparticles.)

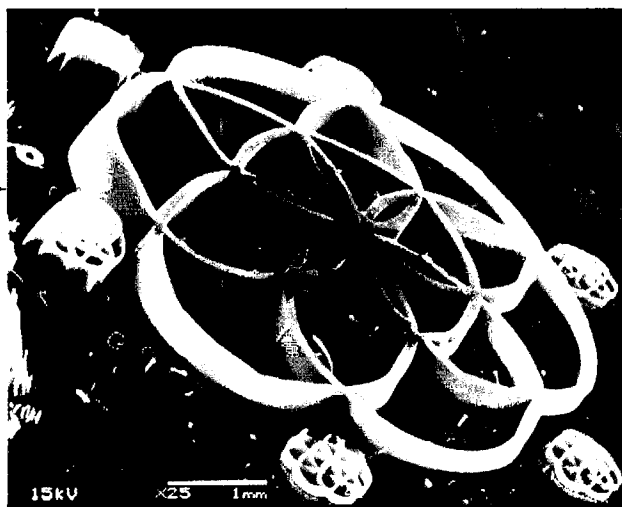
The waters may be further muddied by the lack of stan-

dardized information and accepted best practices for the safe handling of nanomaterials. The expert panel noted that workers traditionally rely on material safety data sheets (MSDSs) provided through the current Workplace Hazardous Materials Information System. But these data sheets only provide information for bulk-scale materials, and not their nanoscale counterparts.

Journey's new company, Maine-based Nanotechnology Toxicology Consulting & Training, will offer toxicology training to businesses with the objective being to eliminate the possibility of undue risk. "There was a survey done in New England with over 80 CEOs, and many of them didn't know where to find the information," he says, emphasizing the need to take science directly to employers.

For now, nanotechnology continues to hold much promise, with scant resemblance to the dreary dystopias imagined by sci-fi writers. Still, from a health and safety perspective, the understanding of nanomaterials and their implications for human health remains a few chapters short.

Umar Abdul is a writer in Toronto.



The Pictures: No Small Feat

Pictures used throughout the article are micro-scale structures of carbon nanotubes (CNTs) as viewed using a scanning electron microscope. CNTs are hollow, cylindrical molecules having exceptional properties, including mechanical stiffness and strength exceeding steel, thermal conductivity exceeding diamond, and unique structure-dependent electrical and optical characteristics. Consequently, CNTs are under investigation for myriad commercial applications. Here, "forests" containing as many as billions of long and parallel CNTs are created by reacting a carbon-containing gas on nanoscale catalyst particles patterned on a silicon wafer. The CNTs self-assemble on the substrate and grow vertically. If a CNT were a tree having 0.5-metre diameter, it would grow at more than 100 metres per second! *Images by A. John Hart, <http://www.nanobliss.com>. Colour added for visual effect.*