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## As Uses Grow, Tiny Materials' Safety Is Hard to Pin Down

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When researchers fashion nanomaterials so small that their dimensions can be measured in molecules, the unusual and potentially valuable characteristics of those materials tend to show up immediately. But as businesses race to exploit those benefits, investors and policy makers are finding that pinpointing the potential environmental and health impacts of nanotechnology could take years.

In fact, the first stages of environmental impact research are generating more new questions than answers.

Take the experience of researchers at DuPont, who are testing microscopic tubes of carbon, known as nanotubes, valued for their extraordinary strength and electrical conductivity. When the researchers injected nanotubes into the lungs of rats in the summer of 2002, the animals unexpectedly began gasping for breath. Fifteen percent of them quickly died.

"It was the highest death rate we had ever seen," said David B. Warheit, the research leader, who began his career studying asbestos and has been testing the pulmonary effects of various chemicals for DuPont since 1984.

Yet surprisingly, all the surviving rats seemed completely normal within 24 hours.

What initially looked like disaster pointed to a possible safety feature: the nanotubes' tendency to clump rapidly led to suffocation for some rats exposed to huge doses, but it also kept most tubes from reaching deep regions of the lung where they could not be expelled by coughing and could cause long-term damage. Now researchers see the clumping of carbon nanotubes and other nanomaterials as a new field for inquiry.

The DuPont research is among the most sophisticated efforts to date to examine potential hazards of nanoscale materials, generally defined as those with at least one dimension less than 100 nanometers (a nanometer is roughly the width of 10 hydrogen atoms). Such materials are already embedded in hundreds of products, including sunscreens and cosmetics, to make them clear; textiles, to make them stain-resistant; and power machinery, to add durability.

Early research has raised troubling issues. DuPont and others, for example, found evidence that the cells that break down foreign particles in rodent lungs have more trouble detecting and handling nanoparticles than larger particles that have long been studied by air pollution experts.

No one has yet created a realistic test for the effects of inhaled nanoparticles; such a test could easily cost more than \$1 million to design and carry out, toxicologists say.

Lungs are not the only concern. Research shows that nanoparticles deposited in the nose can make their way directly into the brain. They can also change shape as they move from liquid solutions to the air, making it harder to draw general conclusions about their potential impact on living things.

"It's going to be 10 years before we can answer the 'so what should I do' question for people," said Eva Oberdörster, an aquatic toxicologist at Southern Methodist University in Dallas. Last month, she began studying how the spherical carbon molecules known as buckyballs are absorbed by water fleas. Eventually, her research could clarify what effects, if any, release of such nanoparticles into the air and water to monitor or control pollution might have on the food chain.

"This field is in its infancy," agreed Joseph B. Hughes, a professor at the Georgia Institute of Technology who oversees environmental engineering research at the Center for Biological and Environmental Nanotechnology, which is at Rice University in Houston. "The first papers and first results will have to be cautious. The field is growing so rapidly in the discovery end that questions about their environmental consequences are still being generated."

Today's nanotechnology applications and those nearing commercialization use tiny amounts of the materials, and for that

reason many entrepreneurs say there is no reason yet for them to investigate potential environmental impacts. DuPont, which has been sued over the health issues of chemicals used in products like Teflon, however, has been more cautious. "It would be unwise to claim that just because there are tiny amounts, it's harmless," said Jim Romine, director for materials science and engineering at DuPont's global research campus outside Wilmington, Del. "We need the data to show that."

At any rate, the amounts being used will not stay tiny for long, if there is any validity to the federal government's projection that sales of products based on nanotechnology will reach \$1 trillion by 2015. That pace of industrial adoption is on a collision course with the measured pace of toxicology and environmental impact research.

Critics like the ETC Group, a technology policy advocacy group, say the current regulatory regime is inadequate, with agencies like the Environmental Protection Agency and the Food and Drug Administration squeezing oversight of the new materials into existing categories. They want development put off until regulators and industry agree on the best practices for handling nanomaterials. Some propose international supervision of research on potential risks.

Nanotechnology advocates say they support faster and broader environmental research, but paying for it has not been a priority for businesses or the government. The Environmental Protection Agency, which until this year had focused on supporting research into how nanotechnology could help clean or protect the environment, is seeking grant proposals from researchers looking at potential risks. But the \$4 million it expects to award next year for risk studies is barely measurable against the \$847 million in federal money that President Bush has proposed for nanotechnology research and development for the 2004 fiscal year.

The difficulty and cost of researching risk are influencing business decisions. L'Oréal, the cosmetics giant, for instance, dropped its research on the characteristics of buckyballs after outside researchers raised questions about toxicity, said Francis Quinn, a physicist in the company's research laboratory in France.

Steven T. Jurvetson, a managing director of Draper Fisher Jurvetson, a venture capital firm that has stakes in nine nanotechnology companies, steers clear of any that raise environmental questions for him. "Until other people's money and research have proven it safe, we'll assume it isn't," he said.

Some smaller nanotechnology start-ups say they simply do not have the resources to push into promising areas that pose health questions. Argonide Nanomaterials of Sanford, Fla., has fashioned alumina ceramic material into fibers just two nanometers thick with superb adhesion characteristics for use in orthopedic surgery, according to researchers at Purdue University.

But Argonide said it preferred to focus on filtering products, which are not implanted in the body and thus require much less testing. The filters, which can remove arsenic from water and recycle water from urine on the International Space Station, will soon be available to filter viruses out of water lines in dental equipment, the company's vice president, Cindi Prorok, said. But what happens to the filters once they are used? Ms. Prorok said she had no idea.

Don't ask, don't tell is the operating mode for much of the nanotechnology industry these days when it comes to where discarded products end up. Many companies assume that because they are working with compounds that are deemed safe in larger sizes or because the nanomaterials are embedded in larger products, the particles will not pose environmental threats.

Even with testing, researchers caution that establishing toxicity is half the challenge. Determining risk also requires projecting how likely animals and people are to be exposed to hazardous materials. Thus, inserting carbon nanotubes in rats' lungs provides data on how toxic they might be but does nothing to answer the question of what level of exposure would be necessary for a rat to breathe in damaging amounts of such particles.

"Our goal is not to look at every individual nanoparticle and say, is this good or is it bad?" said Dr. Hughes at Rice. "There are too many particles, it takes too much time and money and the results are too open to challenge. We are interested in understanding whether they will behave along existing models, and if they differ, what science will help us predict that. There's a growing awareness that it would be an advantage to the industry to study this before the problems manifest themselves."

Photos: David Warheit of DuPont, looking at a microscope slide. He is leading the company's research into the effects of carbon nanotubes on the lungs of rats. (Photo by Tim Shaffer for The New York Times)(pg. C1); Research is looking into how water fleas absorb a type of carbon molecule.; Eva Oberdörster of Southern Methodist University holding a beaker with water fleas. (Photographs by Mark Graham for The New York Times)(pg. C4)