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Getting Nanotechnology Right the First Time

Government and industry should be working to identify and manage possible health and environmental risks before new products are widely used.

Nanotechnology—the design and manipulation of materials at the molecular and atomic scale—has great potential to deliver environmental as well as other benefits. The novel properties that emerge as materials reach the nanoscale (changes in surface chemistry, reactivity, electrical conductivity, and other properties) open the door to innovations in cleaner energy production, energy efficiency, water treatment, environmental remediation, and "lightweighting" of materials, among other applications, that provide direct environmental improvements.

At the same time, these novel properties may pose new risks to workers, consumers, the public, and the environment. The few data now available give cause for concern: Some nanomaterials appear to have the potential to damage skin, brain, and lung tissue, to be mobile or persistent in the environment, or to kill microorganisms (potentially including ones that constitute the base of the food web). This trickle of data only highlights how little is known about the environmental and health effects of engineered nanomaterials. (A bibliography of references and abstracts of risk-related research studies on nanomaterials is available at www.environmentaldefense.org/go/nano.)

As illustrated by the problems caused by asbestos, chlorofluorocarbons, DDT, leaded gasoline, PCBs, and numerous other substances, the fact that a product is useful does not ensure that it is benign to health or the environment. And if the danger becomes known after the product is widely used, the consequences can go beyond human suffering and environmental harm to include lengthy regulatory battles, costly cleanup efforts, expensive litigation quagmires, and painful public-relations debacles. So far, rapid development and commercial introduction of nanomaterials in varied applications are outpacing efforts to understand their implications, let alone ensure their safety. Fortunately, nanotechnology development and commercialization are still at an early stage, so it is not too late to begin managing this process wisely.

Nanotechnology offers an important opportunity to apply the lessons from prior mistakes by identifying risks up front, taking the necessary steps to address

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them, and meaningfully engaging stakeholders to help shape this technology's trajectory. There is an opportunity to get nanotechnology right the first time.

Reason for concern

Nanoparticles can be naturally occurring or generated as byproducts of chemical reactions such as combustion. But attention now is focusing on the large number of engineered nanomaterials—fullerenes (also known as buckyballs), carbon nanotubes, quantum dots, and nanoscale metal oxides, among others—that are beginning to reach the market in growing quantities and in a wide variety of applications.

Studies performed to date are inadequate to provide a full picture of the risks of these engineered nanomaterials and leave open even more questions about other variants and types of engineered nanomaterials. Even so, they offer reason for concern. Studies have demonstrated that some nanomaterials can be mobile or persist in the environment and can be toxic to animals as diverse as fish and rats. A recent Rice University study of buckyballs found that although individual buckyballs do not dissolve well in water, they have a tendency to form aggregates that are both very water-soluble and bacteriocidal, a property that raises strong concerns about ecosystem impacts, because bacteria constitute the bottom of the food chain in many ecosystems. In addition, nanoparticles are deposited throughout the respiratory tract when inhaled. Some of the particles settle in the nasal passages, where they have been shown to be taken up by the olfactory nerves and carried past the blood-brain barrier directly into brain cells. Nanoparticles in the 30- to 50-nanometer range have been shown to penetrate deeply into the lungs, where they readily cross through lung tissue and enter the systemic circulation. This potential for rapid and widespread distribution within the body offers promise of a new array of diagnostic and therapeutic applications for these substances, but it also heightens the importance of having a full understanding of their toxicity.

A variety of nanomaterials have the capacity to cause tissue and cellular damage by causing oxidative stress (the same type of damage that people take antioxidant pills to protect against). Buckyballs caused oxidative damage to brain and liver cells in a study in largemouth bass; other nanoparticles have also been shown to cause oxidative stress in skin cells and in the liver. Most research has used prototypical or "plain" nanoparticles, such as uncoated buckyballs and carbon nanotubes. The few studies that have looked at the effects of variations and coatings have shown that these changes modify the toxicity of the original particle, further complicating the picture and raising the question of how these coatings may degrade over time within the body or in the environment. Oxidative stress may also be part of the mechanism behind the damage to lung tissue that has been observed in several studies of carbon nanotubes. Carbon nanotubes instilled into the lungs of rats and mice have caused unusual localized immune lesions (granulomas) within 30 days, and a separate aspiration study noted this effect as well as dose-dependent lung fibrosis throughout the lung tissue. These and other studies suggest that some nanomaterials can evade the lung's normal clearance and defense mechanisms.

Although the doses and methods of administration used in these studies may not perfectly mirror likely exposure scenarios, these studies strongly suggest the potential for some nanomaterials to pose significant risks.

Urgent need for action

These initial studies highlight how little is known about the health and environmental effects of engineered nanomaterials. Thousands of tons of nanomaterials are already being produced each year, and hundreds of products incorporating nanomaterials are reportedly already on the market. The global market for nanotechnology products is expected to reach at least $1 trillion over the next decade. Given the length of time it will take to develop an adequate understanding of the potential risks posed by a wide variety of nanomaterials and to apply this knowledge to inform appropriate regulation, it is imperative to take action now.

Both the public and private sector's best interests are served by an investment to identify and manage potential risks from nanomaterials now, rather than waiting until problems arise and then struggling to remediate or otherwise cope with them. History demonstrates that embracing a technology without a careful assessment and control of its risks can be extremely costly from both human and financial perspectives. The failure to sufficiently consider the adverse effects of using lead in paint, plumbing, and

gasoline has resulted in widespread health problems that continue to this day and burden us with extremely high cleanup costs. Asbestos is another example where enormous sums of money are being spent by private companies for remediation, litigation, and compensation, even beyond that spent by the public sector to alleviate harm to human health and the environment. Standard & Poor's has estimated that the total cost of liability for asbestos-related losses could reach $200 billion.

The risks at issue here are not only those related to health and the environment but also risks to the very success of this promising set of technologies. If the public is not convinced that nanomaterials are being developed in a way that identifies and minimizes negative consequences to human health and the environment, a backlash could develop that delays, reduces, or even prevents the realization of many of the potential benefits of nanotechnology. As demonstrated with genetically modified organisms just a few years ago, rapid commercialization combined with a failure to address risks early on can lead to product bans and closed markets, resulting in that case in hundreds of millions of dollars in annual export losses for U.S. farmers and companies.

Timely implementation of the following four actions will allow for the most efficient and safest use of nanotechnology.

Increase risk research. The U.S. government, as the largest single investor in nanotechnology R&D, needs to spend more to assess the health and environmental implications of nanotechnology and ensure that the critical research needed to identify potential risks is done, and done expeditiously. Of the roughly $1 billion that the federal government spends annually on nanotechnology, spending for environmental and health implications research accounted for only $8.5 million (less than 1 percent) in fiscal year (FY) 2004 and is proposed to increase to only $38.5 million (less than 4 percent) for FY 2006.

Environmental Defense has called on the U.S. government to increase federal funding for nanomaterial risk research under the National Nanotechnology Initiative (NNI) to at least $100 million annually for the next several years. Although an annual expenditure of $100 million is a significant increase over current levels, it is still a small fraction of the overall federal budget for nanotechnology development. Moreover, it is a modest investment compared to the potential benefits of risk avoidance and to the $1 trillion or more that nanotechnology is projected to provide to the world economy by 2015. Given the complexity of the task, the scope of the necessary research, and available benchmarks for comparison, $100 million per year is a reasonable lower-bound estimate of what is needed.

EPA can and should clarify that nanomaterials are new unless they demonstrably lack novel properties compared to a conventional counterpart.

Broad agreement exists among stakeholders that addressing the potential risks of nanotechnology will be an unusually complex task. Nanotechnology is a potentially limitless collection of technologies and associated materials. The sheer diversity of potential materials and applications, which is a source of nanotechnology's enormous promise, also poses major challenges with respect to characterizing potential risks. Nanotechnology entails many fundamentally different types of materials (and hundreds or thousands of potential variants of each); many novel properties that are potentially relevant to risk; many potential types of applications; and multiple sources and routes of and exposure over the full life cycle of a given material or application.

Even before the research is done that will allow hazards and exposures to be evaluated in detail, a number of more fundamental needs must be addressed. At present, even a basic understanding of which specific properties determine nanomaterials' risk potential is lacking. Many of the methods, protocols, and tools needed to characterize nanomaterials or to detect and measure their presence in a variety of settings, including the workplace environment, the human body, and environmental media, are still in a very early stage of development.

Nor is it clear the extent to which existing knowledge about conventional chemicals can be used to

predict risks of nanomaterials. The defining character of nanotechnology—the emergence of novel properties when materials are reduced to or assembled at the nanoscale—carries with it the potential for novel risks and even novel mechanisms of toxicity that cannot be predicted from the properties and behavior of their bulk counterparts. Risk research is needed to understand nanomaterial characterization, biological and environmental fate and transport, and acute and chronic toxicity.

In each of these areas, existing testing and assessment methods and protocols need to be reexamined to determine the extent to which they can be modified to account for nanomaterials' novel characteristics or need to be supplemented with new methods. Similar challenges will arise with respect to methods and technologies for sampling, analysis and monitoring, all of which will be needed to detect nanomaterials and their transformation products in living systems and in various environmental media.

The view that significantly more money needs to be spent on nanotechnology risk research is further supported by experts' assessments, known testing costs associated with hazard characterization programs for conventional chemicals, and the research budgets for a roughly analogous risk-characterization effort, namely the Environmental Protection Agency's (EPA's) research on risks of airborne particulate matter (PM).

Experts' assessments. Experts from a variety of fields have declared that the NNI's current funding for nanotechnology risk research needs to be significantly increased. Invited government, industry, and academic experts at a September 2004 workshop sponsored by the NNI called for at least a 10-fold increase in federal spending on nanotechnology risk-related research, relative to the approximately $10 million spent in fiscal year 2004. The United Kingdom's Royal Society and Royal Academy of Engineering called for the UK government to devote £5 million to £6 million ($9 million to $11 million) per year for 10 years just to do its part to develop the methodologies and instrumentation needed to set the stage for actual testing of nanomaterials. The chemical industry's "nanotechnology development roadmap," requested by the NNI, indicates that the assessment of hazards to human health and the environment will require a level of cumulative R&D investment that is among the highest of any assigned to the industry's priority research requirements. President Bush's science advisor John H. Marburger III noted that the current toxicity studies now under way through the NNI are "a drop in the bucket compared to what needs to be done."

Hazard endpoint testing costs. Several estimates available from chemical hazard assessment programs can be used to provide at least a lower bound on the costs of testing a nanomaterial for hazardous properties. These costs are for the testing of a conventional chemical for an assortment of hazard endpoints of concern (toxicity plus environmental fate); notably, they do not include costs associated with assessing exposure, which is also needed to assess risk. Generating the Screening Information Data Set, a basic set of hazard information designed to screen chemicals only in order to set priorities for further scrutiny, is estimated to cost roughly $250,000 per chemical. Estimates for filling the more extensive data requirements applicable to high-volume chemicals under the European Union's proposed Registration, Evaluation, and Authorization of Chemicals program exceed $2 million per chemical. The test battery required to register a pesticide under U.S. law can reportedly cost as much as $10 million per pesticide.

EPA research budgets for risks of airborne PM. In response to recommendations from the National Research Council, the EPA spent $40 million to $60 million annually for the first 6 years of a multiyear research program on risks posed by airborne PM. The scope of needed research on nanomaterials is considerably broader and thus likely to cost much more than for airborne PM. This is because airborne PM is a relatively well-studied mixture of chemicals to which exposure arises from a discrete (though highly diffuse) set of sources and through a single route: inhalation. In contrast, nanomaterials

- are composed of many entirely novel, often poorly characterized classes of materials
- will be applied and used in ways that will create the potential for release and exposure through many more pathways, including breathing, ingesting drinking water, and skin absorption
- may be present in wastes, water discharges, and a wide array of products
- may result in the exposure of consumers, as well as the general public and workers, through in-

corporation into products

• pose potential environmental as well as human health risks that need to be considered

Hence, regardless of the ultimate magnitude of risk identified, the research needed to assess the risks is likely to be considerably more involved and costly for nanomaterials than for airborne PM.

The President's Subcommittee on Nanoscale Science, Engineering and Technology already plays a role in coordinating and exchanging information on federal R&D spending for nanotechnology. That coordinating role needs to be enhanced to include the ability to shape and direct the overall federal risk research agenda across agencies to ensure that all critical needs are being addressed, as well as the responsibility and authority to ensure that individual agencies have sufficient resources to conduct the needed research in their areas. In light of the rapidity with which nanomaterials are reaching the market, this added authority is essential to ensure that the right questions are asked and answered on a timely basis.

Out of enlightened self-interest, industry must take the lead in evaluating and managing nanomaterial risks for the near term.

This is not to say that the U.S. government should be the sole, or even the principal, funder of nanomaterial risk research. Other governments are also spending heavily to promote nanotechnology R&D, and they too should allocate some portion of their spending to address nanotechnology risks. And although government risk research has a critical role to play in developing the infrastructure needed to characterize and assess the risks of nanomaterials, private industry should fund the majority of the research and testing on the products they are planning to bring to market. Clearly, all parties will benefit if governments and industry coordinate their research to avoid redundancy and optimize efficiency.

Improve regulatory policy. Although the United States has many regulatory programs in place to address environmental and health risks, those programs are neither comprehensive in their design nor without flaws in their implementation. As a result, some substances can fall through regulatory cracks and go unregulated or underregulated, posing risks that are not discovered until adverse effects are widespread. There are signs that some nanomaterials may be poised to fall between those cracks. Consider a few examples:

• For many substances and products, there is little or no governmental review before they are marketed; regulation occurs only after a problem has arisen.

• Other programs are triggered only if a substance is considered "new." Yet at least some nanomaterial producers are apparently proceeding on the assumption that their products are not new despite their novel properties, and government agencies have not clarified the regulatory status of these materials. As a result, nanomaterials with novel properties are entering commerce without the scrutiny of potential health and environmental effects they warrant.

• Some programs for "new" substances have historically required very limited data to be submitted by producers, relying instead on extrapolation from information on existing chemicals, an approach that is highly questionable for nanomaterials, given how few hazard data now exist.

• Under many regulatory programs, coverage is triggered by mass-based thresholds or standards. Yet because of their high surface-area-to-mass ratios or other properties, nanomaterials often exhibit dramatically increased potency or other activity relative to their bulk counterparts, a distinction not reflected in existing mass-based measures.

• Some potential nanotechnology applications may fall through the cracks between the jurisdictions of multiple regulatory programs. For example, sunscreens using nanoparticles of titanium dioxide were reviewed by the Food and Drug Administration (FDA) for potential immediate health effects on consumers, but neither the FDA nor the EPA reviewed how titanium dioxide nanoparticles may affect aquatic ecosystems when these sunscreens wash off.

At this point, federal agencies need to vigorously use their existing statutory authorities to address potential nanomaterial risks as effectively as possible. Regrettably, there are few signs of action on this score.

For example, the EPA has been conspicuously silent regarding the extent to which nanomaterials are "new" or "existing" chemical substances for purposes of the Toxic Substances Control Act, an important distinction because only new chemicals trigger premanufacture notification and review requirements. The EPA can and should clarify the principle that nanomaterials are new unless they demonstrably lack novel properties as compared to a conventional counterpart. Further, the EPA should clarify that nanomaterials do not automatically qualify for the exemptions from premanufacture notice provisions that are allowed for materials produced in low volumes or thought to result in low exposure, at least until appropriate nanomaterial-specific definitions of "low volume" and "low exposure" can be set. Likewise, before assuming that the existing exemption of polymers from the premanufacture notification program applies to nanomaterials, the EPA needs to determine whether nanomaterials meet the rationale for the exemption; namely, that the molecules are too large to be biologically available and that they degrade only into substances that have already been evaluated. The EPA should also state publicly that it is unlikely to approve the commercial manufacture of a nanomaterial in the absence of hazard and exposure data sufficient to characterize its potential risks.

As agencies apply their existing authorities (or fail to do so), the need for further steps may well become evident. A comprehensive and independent process that identifies deficiencies as well as steps to address them will be vital.

Develop corporate standards of care. Even under the most optimistic scenario, it appears unlikely that federal agencies will put into place adequate provisions for nanomaterials quickly enough to address the materials now entering or poised to enter the market. Out of enlightened self-interest, industry must take the lead in evaluating and managing nanomaterial risks for the near term, working with other stakeholders to quickly establish and implement life cycle-based "standards of care" for nanomaterials.

These standards should include a framework and a process by which to identify and manage nanomaterials' risks across a product's full life cycle, taking into account worker safety, manufacturing releases and wastes, product use, and product disposal. Standards of care should also include and be responsive to feedback mechanisms, including environmental and health monitoring programs to check the accuracy of the assumptions about a material's risks and the effectiveness of risk management practices. Such standards should be developed and implemented in a transparent and accountable manner, including by publicly disclosing the assumptions, processes, and results of the risk identification and risk management systems.

Ideally, such standards of care would help provide a model for sensible regulatory policies as they emerge. This would assure the public that all companies, not just those who participate in voluntary programs, are taking the steps needed to safely manage nanomaterials. This would also set a level playing field for companies, so that responsible companies are not at a disadvantage relative to those that cut corners.

Engage a diverse range of stakeholders. To date, neither government nor industry has sufficiently engaged the wide array of stakeholders—including labor groups, health organizations, consumer advocates, community groups, and environmental organizations—whose constituencies both stand to benefit from this technology and are most likely to bear any risks that arise. Government and industry need to engage these various stakeholders and consider their views in deciding how to develop and manage this promising technology in a way that maximizes its benefits and minimizes its risks.

All too often, "stakeholder involvement" translates in practice into either communicating the end result of a process to those who have been excluded (whether intentionally or by default) from participating in it, or seeking to "educate" the public in order to promote a technology and allay concerns that the technology's proponents believe to be unfounded. Engagement is not simply top-down communication. It means involving stakeholders from the outset in helping to identify expectations and concerns, and providing a role for them in helping to set priorities for research and action. And many of these stakeholders not only have a stake or interest in nanotechnology, they also have relevant perspective, experience, and expertise to offer.

Here again, there is an opportunity to get this right the first time. The potential payoff in terms of reduced risks and increased market and public acceptance will almost certainly greatly exceed the investment necessary to draw these important voices into

the discussion.

The rapid commercialization of nanotechnology, coupled with the potential risks from at least certain nanomaterials as demonstrated in initial studies, lend urgency to the need for government and industry to direct more of their investments in nanotechnology development toward identifying the potential risks and addressing them. Government and industry have done a great job so far in accentuating nanotechnology's potential up sides and in accelerating its development, but they have yet to come to terms with their equally critical roles in identifying and avoiding the down sides. A far better balance between these two roles must be struck if nanotechnology is to deliver on its promise without delivering unintended adverse consequences. With the right mix of increased risk research, improved regulatory oversight, self-initiated corporate standards, and inclusive stakeholder engagement, we have the opportunity to get nanotechnology right the first time.

"I'm on board for microbrews, but nanopizza is taking technology a step too far."