

Opportunities and Threats from Nanotechnology in Health, Food, Agriculture and the Environment

Ricardo Molins¹

Abstract

Nanotechnology, a relatively new field of research and industrial materials development based on the creation of new classes of novel molecular structures, is making rapid advances that promise to radically change or influence many fields of science and technology. The development of various types of nanomaterials for application in revolutionary medical treatments, agricultural research and food safety diagnostic methods, new environmental remediation procedures, energy applications like solar cell coatings, and even high-volume, everyday products such as cosmetics, dirt-repelling fabrics, and self-cleaning paint, offer innumerable possibilities for human progress. However, it is essential and urgent to assess not only the benefits but also the potential risks posed by nanoparticles, and agree on effective measures to prevent such risks through appropriate regulatory approaches.

¹ Director of Agricultural Health and Food Safety at IICA. ricardo.molins@iica.int



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What are Nanotechnology and Nanomaterials?

Nanotechnology, from the Greek “nano,” for dwarf, consists of manipulating materials at the atomic and molecular levels to create new molecular structures known as “nanomaterials” having unique and new characteristics that differ from those of the original materials they are derived from. These materials belong to several classes that vary from each other in many basic characteristics such as persistence, reactivity, and behavior in biological systems, to an extent that makes it impossible to generalize about their properties.

Nanotechnology promises to change the world, as we know it, in many ways; for example, from self-cleaning car paint and clothes that never absorb dirt or odors to drug delivery systems able to target specific organs. Nanomaterials are already being produced and marketed and their use in a myriad of applications is only a matter of time. Nanotechnology is taking miniaturization to the ultimate level, the building blocks of nature, where the physical and chemical behaviors of materials are no longer the same. The confluence of nanotechnology with molecular biology and information technology, combined with revolutionary

developments in instrumentation, is opening the door to a new industrial age bordering on science fiction. Recognizing the immense potential of this new field, governments across the world are investing heavily in nanotechnology research in order to stake out a competitive position (Thayer 2002). For example, a National Nanotechnology Initiative (NNI) has been implemented in the United States to promote this technology (NNI 2007).

To place nanomaterials in context, consider that the size of atoms is in the 0.1-1 nanometer (nm) range, whereas simple molecules may be somewhere between 1 and 10 nm, viruses between approximately 10 and 100 nm, and bacteria between 1 and 10 micrometers (μm) (Warad and Dutta 2007). Particles smaller than 50 nm follow quantum physics, whereas classical physics laws apply to larger particles. At the nanoparticle level, changes in electrical, chemical, magnetic, mechanical or biological properties of materials can occur that differentiate them from the corresponding bulk material, albeit with no change in chemical composition. Materials may present new, enhanced characteristics such as flexibility, strength, conductivity, surface tension, and even color when the particles become smaller than 100 nm. However, they also may increase in chemical



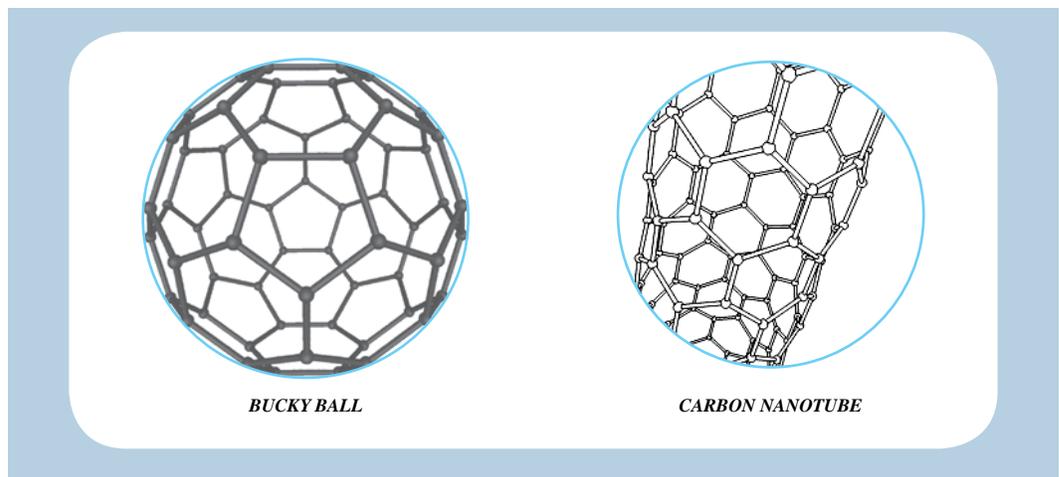
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² One nanometer is one-millionth of a millimeter.

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reactivity because of increased surface area to mass ratio. As more atoms are exposed to the exterior, particularly in crystalline nanoparticles, they are more loosely bound and hence more likely to react.

In contrast to traditional material science, which relies mostly on breaking materials down to particles to regenerate them or create new materials, nanotechnology builds materials through self-assembly, beginning with atoms. Truly new materials are being created through the designed arrangement of atoms into nanostructures of various types. “Bucky balls,” for example, also called Buckminster fullerenes, are carbon-based nanostructures configured in ways similar to geodesic domes and resembling soccer balls.



Another type of nanostructure, called “nanotube,” is being manufactured as the building block of new, highly flexible yet extraordinarily strong carbon-based fibers. Nanotubes are hollow cylinders having diameters in the nanoscale range of 1 to 100 nm. Carbon nanotubes, one of the few nanomaterials currently being produced in large volumes, present some unique properties that include high conductivity, high molecular adsorption capacity, and high tensile strength. These

characteristics of carbon nanotubes are being tested for application in fields as diverse as nanoelectronics, optical communications, aviation building materials, laboratory diagnostics, and fuel cells.

Modification of existing materials also offers seemingly limitless opportunities for nanotechnology. Nanoparticles for use in such applications as scratch-resistant glass or plastic, or as additives

in self-cleaning paint for cars and street signs, buildings, and solar cell surfaces, and dirt-repelling clothes are also in the making. Currently, nanoparticles are being used in such diverse applications as making metal surfaces impervious to corrosion and producing clear sunscreen creams.

The Opportunities and Promises of Nanotechnology

Nanotechnology in Medicine

Nanotechnology presents an immense potential to advance many sciences. One of the most visible and potentially most immediate and promising applications of nanomaterials are in medical diagnosis, treatment, and prevention of diseases such as cancer. The vast trove of information generated by the Human Genome Project has brought about advances in cancer genomics and proteomics that, combined with nanotechnology, may revolutionize oncology by manipulating the molecular basis of cancer. To this end, the National Cancer Institute (NCI) of the United States developed a *Cancer Nanotechnology Plan* (CNPlan) and formed a working group, the NCI Alliance for Nanotechnology in Cancer. This comprehensive plan covers the areas of cancer prevention and control, early detection and proteomics, imaging diagnostics, multifunctional therapeutics, and quality enhancement in cancer care (United States Department of Health and Human Services *et al.* 2004)).



In vivo diagnostic applications of nanotechnology, such as magnetic resonance imaging (MRI) contrast agent delivery to cancer cells via nanodevices, could make it possible to detect cancer at very early stages. *In vitro* diagnostics, in turn, is benefiting already from the use of nanoscale cantilevers able to increase the sensitivity of detection methods down to a single molecule for such cancer markers as specific proteins.

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Nanotechnology in Agriculture, Food and the Environment

Because nanoscale devices or components of larger devices are much smaller than human, animal or plant cells, they may be used to gain access to the inside of cells. This would allow researchers to observe and measure transport of proteins within the cell, for example, as well as to measure gene expression. This opens up a completely new horizon in health and agricultural research in areas such as animal and food plant genetics and conversion of wastes into energy (Thayer 2002; Joseph and Morrison 2006).

Bucky balls, for example, could be coated with antibodies specific to selected organs or cells in the human body and their interior filled with such pharmaceuticals as chemotherapy drugs or therapeutic substances. Once injected into the human or animal body, the bucky balls would act as targeted drug delivery systems that would search for, and eventually gather at and deliver their content to, the targeted organ or cells only. Furthermore, the same drug-delivering nanodevice could carry a tagging contrast agent that would allow confirmation of drug delivery through imaging techniques (Hett 2004).

Other such structures could themselves be targets for magnetic activation to generate localized, tumor-killing heat through high-frequency vibration. Combinations of these capabilities within a single nanodevice have given rise to the concept of the "nanoclinic."

An example of the potential of nanoparticles to penetrate cells is that of a nano-herbicide - under development jointly by agricultural research institutes in Mexico and India - that would attack a weed's seed coating (Roach 2006b)). Germination would be prevented and the seed would thus be destroyed even when it is buried deep in soil, below the reach of tillers and conventional herbicides, because soil particles would not be able to stop the minute herbicide nanoparticles from migrating down.

Other applications for rapid, portable, simultaneous detection of pathogenic bacteria such as *Salmonella* spp., *Escherichia coli* O157:H7 and *Listeria monocytogenes* in foods are in development. Food samples would no longer have to be sent to laboratories, since the analyses would be done at the farm, slaughterhouse or processing plant or during transport.

According to the researchers working on this method of analysis (Roach



2006a)), the process uses nanowires and antibodies so that the presence and type of contamination and its concentration can be simultaneously determined. Individual nanowires are assigned a recognizable pattern of silver and gold stripes akin to a nano-barcode and set on a strip. Specific pathogen antibodies are then attached to each nanowire. For example, nanowire-one could have the antibody to *Salmonella* and nanowire-two the antibody to *E. coli*. During use, these strips are placed on the meat or other food and if *Salmonella* is present, the cells will bond with the corresponding antibody on nanowire-one.

Detection is made possible by using a fluorescent solution that contains a multitude of antibodies. The nanowires are then exposed to the fluorescent antibodies cocktail and the pathogens, already bonded with antibodies on the nanowires, will also bond with the corresponding fluorescent antibodies in what is known as a "sandwich immunoassay." Because each nanowire is recognizable by its gold and silver striped pattern, an electronic processor will instantly be able to tell which pathogens are present and in what

concentration. According to another group of researchers working on a similar system, detection time could be as little as 15 minutes (El Amin 2006).

In addition, light emitting nanoparticles linked to antibodies may be used to develop assays capable of simultaneously detecting multiple chemical substances, something that may find invaluable applications in toxicology such as multiple pesticide residue detection and quantification (Thayer 2002; Joseph and Morrison 2006). This type of assay would be invaluable to determine the safety of foods.

In environmental protection, nanotechnology is finding applications in photocatalysis, a process in which light promotes a reaction between compounds such as pesticide residues and the nanomaterial without the latter being consumed. Such a process would be useful in decontamination of water for agricultural and human use. For example, elimination of oils, agrochemicals and waste products - including biological contaminants such as viruses - via photocatalysis, using nanomaterials made of titanium oxide (TiO_2), has been widely and successfully

studied. In food safety, photocatalysis could find uses in cleansing the surface of fresh fruits and vegetables of toxic agrochemical residues and in destroying bacteria on such produce (Joseph and Morrison 2006).

In the area of agricultural production and marketing, Warad and Dutta (in Thayer 2002) make a good case for future application of nanomaterials in nano-barcodes. These invisible barcodes could be extremely useful for tagging fruits, vegetables and many other agricultural products at the farm, for subsequent electronic traceability throughout the food chain all the way to the consumer. Such miniature barcodes would be totally unobtrusive and thus nearly impossible to tamper with, and electronically readable.



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The threats. The potential hazards posed by nanomaterials are largely unknown

Will the public accept nanotechnology? The experience of atomic energy and agricultural biotechnology provides important lessons. In the U.S., the adverse public reaction to nuclear energy has hindered its development even though it is widely used in Europe and the rest of the world. Risk communication experts have pointed to aspects such as the invisibility of radiation and the fact that cancer is a “dread disease” to explain the opposition to atomic energy in the U.S.; however, the fact is that no new nuclear plants have been built for decades.

In Europe, the public has negatively responded to agricultural biotechnology (but not the use of biotechnology in manufacture of pharmaceuticals and chemicals). While nanotechnology products already are entering the market, there is also much in the popular mind to create negative perceptions, such as science fiction and a horror film depiction of non-existent “self replicating” nanotechnology particles.

To replace irrational responses with rational ones requires the generation of information, not only about the benefits but also about the potential risks posed by nanoparticles, and agree on effective measures to prevent such risks through appropriate regulatory approaches (Michelson, undated, on line). From the past we have also learned that involvement of stakeholders - industry, government, consumers and the medical community - is essential to assure that the right



questions are asked, that information is shared and that decisions are informed by the concerns of all involved and not imposed on the public without their consent.

A starting point is to begin to understand some of the potential hazards. Not much is known. We do know that some of the characteristics of nanomaterials that make them so desirable in various applications may also pose new safety challenges. For example, as a result of changes in reactivity at the nanoscale level, the well-known toxicological behavior of common materials such as carbon, described in material safety data sheets (MSDS) for the bulk material, no longer applies (Colvin 2003). Moreover, unlike such natural nanoparticles as salt particles in marine aerosols, which are soluble, and insoluble but short-lived combustion-generated nanoparticles that have a tendency to aggregate to form larger particles, manufactured nanoparticles are often purposefully coated with substances that prevent agglomeration. This coating

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is often required because the small size of nanoparticles would promote strong aggregation once the particles are withdrawn from the liquid phase or enclosed gas phase used for manufacturing them. Thus, such coated particles may remain in their original, highly reactive form in the environment or the human body for an undetermined period of time.

Because of the very small size of manufactured nanoparticles, and particularly because of surface treatments designed to preclude nanoparticles from agglomerating into larger particles, it is



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likely that many nanomaterials entering the environment would remain in it indefinitely (Colvin 2004). Surface coatings have been shown to produce highly mobile nanoparticles, whether in the air, soil, or water. Airborne nanoparticles do not tend to settle onto surfaces and may not be retained by common respirator filters. Once deposited on soils, nanoparticles can not only traverse various strata and find their way into aquifers, but current drinking water filtering systems might not filter out many of them. Some hydrophobic nanomaterials can also form a stable colloidal species in water even when not surface treated (Alargova and Tsujii 2001). The potential hazards posed by these particles moving freely in the environment, therefore, are new to humankind.

The mobility of manufactured nanoparticles is not limited to the environment. Unlike other, naturally occurring nanoparticles that are soluble, such as saline particles, manufactured nanoparticles do not dissolve upon entering the human lungs. In addition, unlike other nanoparticles originating as byproducts of combustion engines and processes, manufactured nanoparticles, by design, would not agglomerate as much and thus could remain more reactive for longer periods of time. Instead, their very small size would allow them to enter the human bloodstream via the lungs after inhalation,

the digestive tract if ingested, and even the skin if applied or deposited on it, as with sunscreens already in the market.

There may be novel routes of exposure as well; one specific type of nanoparticle has been shown to enter the brain via the olfactory system. Once in the bloodstream, nanoparticles have been shown to be able to reach all organs of the human body. Just as this property may present unique opportunities for new medical treatments, it also presents the potential for unintentional accumulation of such particles in brain and other human tissues, calling for the urgent need to conduct research on possible adverse effects.

Certain nanotubule structures have been found to cause oxidative damage to human skin cells in culture (Shvedova *et al.* 2003). There are published reports on the adverse effects of certain carbon nanotubes infused into the lungs of mice. Responses for carbon nanotubes were more severe than the response for quartz, a known occupational hazard that was used as a positive control. With long-term exposure, there was lung necrosis and scarring (Lam *et al.* 2004). Such experiments have yet to be performed for other nanotube structures as well as other materials that already are on the market. Might there be a parallel between the toxic mechanism of this particular type of carbon nanotube in the lungs with that of asbestos, based on the nature of the pathologic response?

Whether these particular nanotubes would represent a hazard for those working in manufacturing plants is unknown. Research involving controlled clinical and animal studies using ultra-fine elemental carbon particles reported high deposition

of the particles in the human respiratory tract (ICRP 1994). These particles escaped phagocytosis by macrophages and were translocated to organs other than the lungs. Cardiovascular effects in humans and animals and mild inflammatory processes in animals were also observed. Another type of similar particles, delivered intravenously, was able to cross the blood-brain barrier (Kreuter 2001) and a possible mechanism for transport of such particles from lungs to other tissues has been proposed (Oberdörster and Utell 2002).

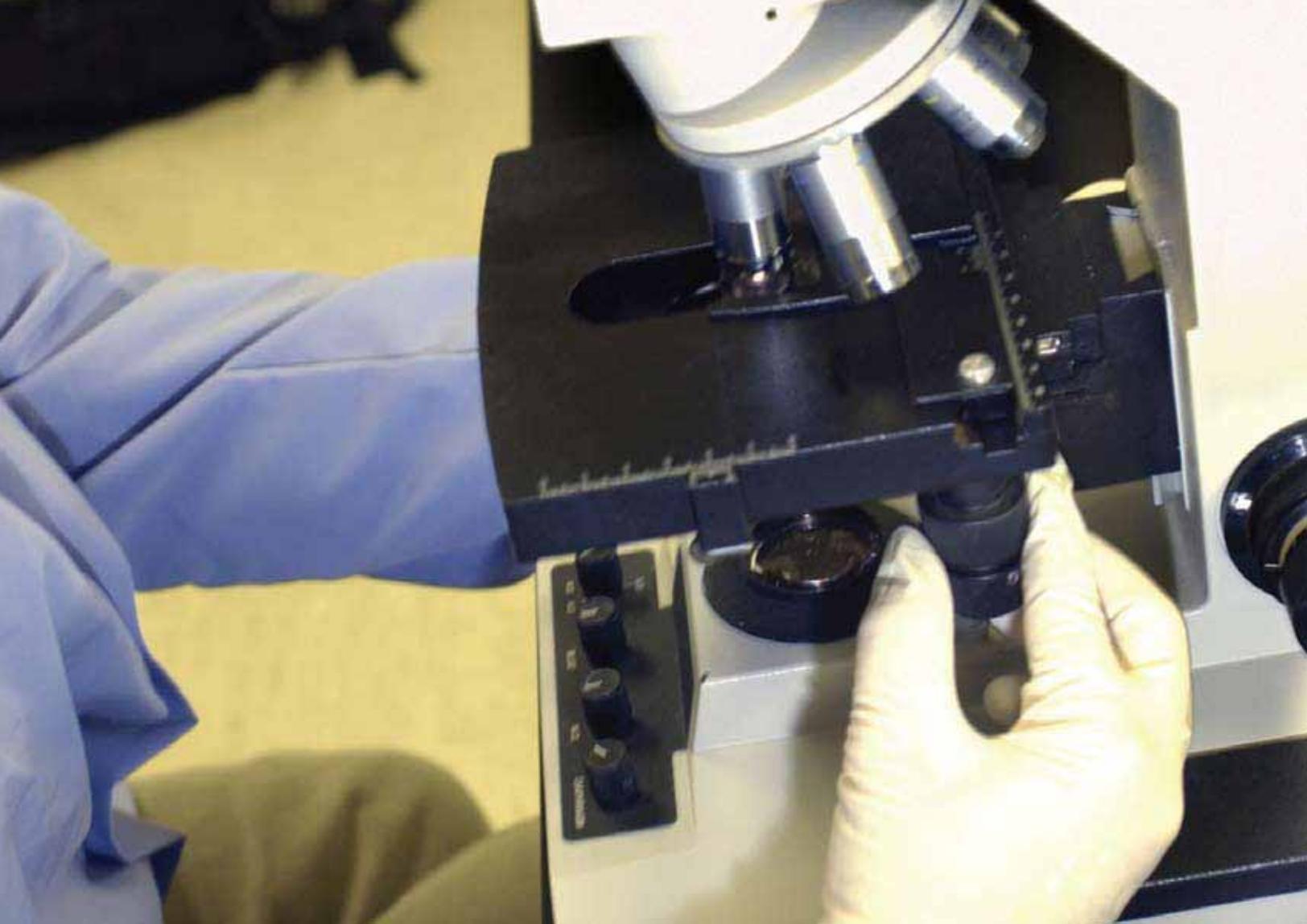
The above studies, however, did not deal with the various potential direct and indirect routes of human exposure to nanoparticles or with the ecological fates and transports and environmental lifecycles of such materials. Nanomaterials used in agriculture and foods would enter the human body via the digestive tract, as would those contaminating ground water. Very little is known about these issues, despite the fact that the future of nanotechnology itself may hinge on them. Early results indicate that certain types of nanoparticles may cause exposure via novel routes. In 2004, Oberdörster reported that fullerenes (C₆₀) suspended in water may have been directly transported to the brains of fish via olfactory neurons (as is known to occur for other small substances such as viral particles) (Oberdörster 2004).

As pointed out by Colvin (2003) in a report on the potential environmental impact of engineered nanomaterials, nanotechnology is developing and nanomaterials are being commercialized without any government oversight. Workers employed in plants manufacturing nanomaterials are likely exposed to them but so are workers who use such products, for example, painters who



use nanotechnology-derived spray paints or cosmeticians who use nanotechnology cosmetics every day. However, because current Material Safety Data Sheets (MSDS) for nanomaterials list the same properties and restrictions given for the bulk material, no additional or special requirements for safety precautions are mentioned.

The United States National Institute for Occupational Safety and Health (NIOSH) estimates that up to two million workers are currently exposed through work in nanotechnology industries in the United States and at least another million workers could be so exposed in the coming ten years. No guidelines for employers have so far been issued by the Occupational Safety and Health Administration (OSHA) (Gruenwald 2004). NIOSH, recognizing the current information gap regarding the potential health effects of nanomaterials, is working with an interagency nanotechnology group to develop guidelines for dealing



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with nanomaterials released in the workplace. Also participating in drafting of the guidelines will be OSHA and a working group of the Nanoscale Science, Engineering and Technology Subcommittee (NSET) of the U.S. National Science and

Technology Council. In addition, the U.S. Department of Defense has funded the development of a computational model to predict toxic, health, and biocompatible effects of nanomaterials on the basis of the structure of nanoparticles (DoD 2004).

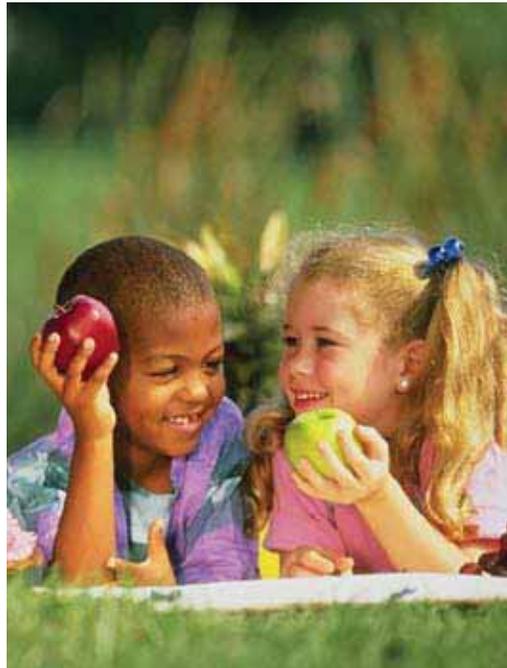
Regulating Nanotechnology. The need for leadership and trust

The issue of regulating the growing nanotechnology industry is not a simple one. The field is quite extensive, both from the standpoint of variety of materials as well as from that of applications. In addition, there can be no sensible regulations unless the risks posed by these materials and techniques have been assessed, and there are few data to support such assessment. Furthermore, there are no clear guidelines to assess the risks posed by nanomaterials, and there is not even agreement on a common nomenclature for these materials and techniques that would make specific regulations clear to all concerned parties.

Because of the immense scope of this technology, it has been said that “regulation of nanotechnology is a process, not an event.” The applicability of the U.S. Toxic Substances Control Act (TSCA) to new nanomaterials has been the subject of debate. An extensive study on the subject was unable to confirm that the law, in its present form, was sufficient to meet the challenges posed by the growing nanotechnology industry (Bergeson 2006).

It may be argued that the “precautionary principle” should be applied, and that further development of nanotechnology should be put on hold until the potential hazards posed by nanomaterials to humans and the environment are better understood. However, such an approach might not be practical or even realistic any longer because the fundamentals of nanotechnology are already in the public domain. Prohibition

would also be devastating to and opposed by many scientists and entrepreneurs who are fully committed to developing a truly promissory technology. However, it could also be argued that a precautionary approach should especially be applied for applications that are dispersive, and that may cause persistent and irreversible long-term environmental impacts. If we have learned any lessons from the past, it is surely that development that is not sustainable is, in the long run, most damaging to economic progress. Policies will need to strike an appropriate balance between technological advancement in this area and avoidance of long-term threats to health and the environment.





► *Therefore, a determined but coordinated commitment to ascertain and anticipate adverse health and environmental effects of nanomaterials by all parties involved in nanotechnology development - academia, government, and the private sector - is essential to avert the emergence of public distrust and rejection of nanotechnology that doomed or at least slowed down the development of other novel technologies.*

Therefore, a determined but coordinated commitment to ascertain and anticipate adverse health and environmental effects of nanomaterials by all parties involved in nanotechnology development - academia, government, and the private sector - is essential to avert the emergence of public distrust and rejection of nanotechnology that doomed or at least slowed down the development of other novel technologies. Regulators need to show concern and offer guidelines and coordination, while researchers must develop ethics that emphasize self-regulation, culture and expectations (Schultz 2002). Appropriate communications, including disclosure of negative as well as positive findings, will be critical in establishing the kind of public confidence in nanotechnology that was lacking during development of other technologies.

Conclusions

Nanotechnology presents enormous potential to improve human life. However, little is known about the risks posed by nanomaterials to human health and the environment and the technology is developing in a mostly unregulated manner. Therefore, to set the appropriate scientific background for studying the optimal approach to regulating nanotechnology and nanomaterials, urgent actions are needed in several areas. Some of the actions that should be taken to address the situation are summarized below, in order:

1. A common, harmonized glossary of definitions and terms specific to this new technology must be developed and agreed upon on a global basis, so that everyone will use a common technical nanotechnology vocabulary.
2. Reference standards for nanomaterial types and sizes must be developed and made available, so that toxicologists and other researchers may access standardized materials and develop standard analytical methods.

3. Research on exposure routes to and life cycles of manufactured nanomaterials is urgently needed to support scientifically sound risk assessment of the potential health and environmental hazards posed by such materials. In addition, appropriate human health and ecological risk assessment methodology for nanomaterials and nanodevices is lacking and in need of development. These methods should be harmonized and accepted globally.
4. Finally, public participation in a process to develop a reasoned and cautious approach to the assessment and control of nanotechnology risks is called for. Careful *risk communication* should be undertaken, involving governments at all levels, industry, the medical community, researchers and the public.

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Résumé / Resumo / Resúmen

► **Bienfaits possibles et menaces de la nanotechnologie pour la santé, les denrées alimentaires, l'agriculture et l'environnement**

La nanotechnologie, champ relativement nouveau de recherche et d'élaboration de matériaux industriels, fondé sur la création de nouvelles classes de structures moléculaires originales, enregistre des progrès rapides qui promettent de changer radicalement ou de toucher de nombreuses sphères du domaine de la science et de la technologie. Elle ouvre également d'innombrables perspectives pour le progrès humain, avec la mise au point de divers types de nanomatériaux qui trouveront des applications dans des traitements médicaux révolutionnaires, dans la recherche agricole et les méthodes d'évaluation de l'innocuité des aliments, dans les procédés de remise en état de l'environnement, dans le domaine énergétique, par exemple pour le revêtement des cellules solaires, de même que dans des produits d'usage quotidien de grande consommation tels que les cosmétiques, les tissus qui repoussent la saleté et la peinture autolavable. Néanmoins, il est essentiel et urgent d'évaluer non seulement les avantages mais également les risques possibles présentés par les nanoparticules et de s'entendre sur des mesures réglementaires efficaces fondées sur des critères appropriés.

► **Oportunidades e ameaças da nanotecnologia para a saúde, os alimentos, a agricultura e o meio ambiente**

A nanotecnologia, um campo relativamente novo de pesquisa e elaboração de materiais industriais com base na criação de novos tipos de estruturas moleculares originais, mostra rápidos avanços que prometem mudar radicalmente ou afetar muitas áreas da ciência e da tecnologia. Além disso, oferece inúmeras possibilidades para o progresso humano mediante a criação de vários tipos de nanomateriais aplicáveis em revolucionários tratamentos médicos, na pesquisa agrícola e em métodos de diagnóstico de inocuidade alimentar, em procedimentos de restauração ambiental e aplicações energéticas, como o revestimento de células solares, inclusive em produtos corriqueiros de grande volume, por exemplo, cosméticos, tecidos repelentes à sujeira e pintura auto-lavável. Não obstante, é essencial e urgente avaliar não apenas os benefícios, mas, também, os possíveis riscos dessas nanopartículas e concordar medidas efetivas mediante critérios reguladores adequados.

► **Oportunidades y amenazas de la nanotecnología para la salud, los alimentos, la agricultura y el ambiente**

La nanotecnología, un campo relativamente nuevo de investigación y elaboración de materiales industriales con base en la creación de nuevas clases de estructuras moleculares originales, muestra rápidos avances que prometen cambiar radicalmente o afectar muchas esferas de la ciencia y la tecnología. Además, ofrece innumerables posibilidades para el progreso humano, mediante la creación de varios tipos de nanomateriales aplicables en revolucionarios tratamientos médicos, en la investigación agrícola y métodos de diagnóstico de inocuidad alimentaria, en procedimientos de restauración ambiental, aplicaciones energéticas como el revestimiento de células solares, incluso en productos cotidianos de gran volumen como los cosméticos, tejidos repelentes de la suciedad y pintura auto-lavable. No obstante, es esencial y urgente evaluar no sólo los beneficios, sino también los posibles riesgos que plantean las nanopartículas y acordar medidas efectivas mediante criterios reguladores adecuados.