

■ PART I

ENVIRONMENTAL AND HEALTH IMPACTS OF NANOMATERIALS: OVERVIEW AND CHALLENGES

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Nanomaterials and the Environment

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1.1 INTRODUCTION

The use of nanomaterials, manufactured products having one or more dimensions 100 nm or less, has grown dramatically in the last decade and promises to continue to grow in the future. Currently, nanomaterials are used in medical devices, pharmaceuticals, environmental remediation, and in scores of consumer products ranging from cosmetics to electronics, with numerous forthcoming applications (1, 2). Forecasts predict nanotechnology, the science of using nanomaterials and nanodevices, to be a \$10 billion industry by 2010, growing to \$1 trillion by 2015 (3, 4). Figure 1.1 illustrates in graphic form the rapid growth in data found in the literature on nanoproductions via a search of life science journal articles using the terms “nanotechnology,” “nanomaterial,” and “nanoparticle.”

Nanomaterials can be composed of many different base materials and have different structures. A few examples of nanomaterials are listed in Table 1.1 (adapted from Reference (5)). Typical nanomaterials include carbon-based fullerenes (buckminsterfullerene, buckyballs, and C₆₀ fullerenes) and nanotubes, which have been used to selectively target and eliminate cancer cells (6); quantum dots, which are nanoscale semiconductor crystals used to track protein transport in biological systems; metal oxanes, such as titanium oxide (TiO₂) and zinc oxide, which are used in sunscreens for their ultraviolet (UV) reflecting capability in cosmetics, and in the formulation of membranes and films (7); and silver nanoparticles, which are widely incorporated into products such as antibacterial and antifungal elements (8–10).

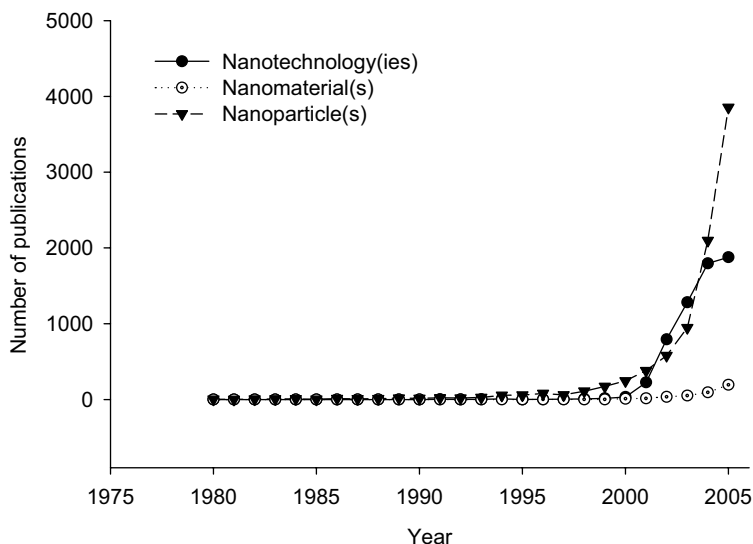


FIGURE 1.1 Growth in Nanotechnology publications: number of nanotechnology-related publications by year from 1990 to 2005 via literature search of life science journal articles on nanotechnology, nanomaterials, and nanoparticles.

What makes nanomaterials unique is their nanometer scale. At this very small size, the properties of materials can change. For example, quantum-mechanical effects can alter the behavior of small particles, such as their light-emitting color and electronic properties. Nanomaterials may have increased chemical reactivity as a consequence of increased surface area to volume ratio, compared to materials with the same chemical composition synthesized at the macroscale. This is because the chemical reactivity of a material depends on its surface area, which increases as the particle size decreases. For instance, gold in its bulk form has been regarded to be chemically inert, especially to

TABLE 1.1 Examples and Characteristics of Nanoproducts

Structure	Size	Base Material	Examples
Tubes	Diameter: 1–100 nm	Carbon	Single-walled carbon nanotubes (SWCNTs), multiwalled carbon nanotubes (MWCNTs)
Wires	Diameter: 1–100 nm	Metals, semiconductors, tellurium nanowires	Silicon nanowires, cadmium oxides, sulfides, nitrides
Crystals, clusters	Radius: 1–10 nm	Semiconductors, metals, metal oxides	Quantum dots, titanium dioxide, silicon dioxide
Spheres	Radius: <100 nm	Carbon	Fullerenes (C ₆₀ , buckyballs)

Adapted from Reference 5.

reactions with oxygen and hydrogen. However, at the nanoscale, gold has been found to be extremely reactive and is extensively being developed as a catalyst for a large range of chemical reactions (11–13).

Because nanomaterials have so many applications, with more to come, the prevalence of these materials in industry and society is ensured. It is evident from past experience that development of innovative products is not always associated with benign consequences in the long term, as illustrated by methyl tertiary butyl ether (MTBE), dichlorodiphenyltrichloroethane (DDT), and chlorofluorocarbons (CFCs), all of which have had significant adverse health and environmental impacts. While the novel properties that arise when a material is reduced to the nanoscale make them useful for a wide range of applications, little is known about how these properties will affect human health or how they will behave in the environment. These novel properties may also confer unusual mechanisms of toxicity and risks that cannot be predicted by existing knowledge or extrapolation from what is known regarding the behavior of these materials at the macroscale (14, 15). The degree of potential exposure to populations is also unknown and, at present, there is a lack of standard risk evaluation and safe handling guidelines for nanomaterials. The potential risks nanomaterial poses promises to be contentious until the uncertainties regarding toxicity and exposure are known.

1.2 NANOMATERIALS AND THE ENVIRONMENT

To address the potential influence of nanomaterials on the environment, assessment of their physiochemical properties will be needed to determine their fate, mobility, degradation, persistence, and bioavailability. The biological effects and the detection of nanomaterials in nature and in any environmentally exposed species, including humans, are also essential elements to consider. Nanomaterial risk assessment must evaluate the following: the toxicity of particular nanomaterials, the extent of their dispersion in the environment, environmental fate and transport, transformations and modifications in the environment that may affect bioavailability, absorption, and toxicity upon exposure to biological systems, biological and ecological relevance of exposure, acute versus low level chronic exposure, and the ability to determine and measure exposure to the environment and to biological systems. In humans, the extent of exposure in several settings will need to be considered. These include exposure from occupational, commercial, and environmental sources. Given the bulk of knowledge needed for a proper assessment of the growth of nanoparticle use and manufacture, it seems that there will always be a lag in research as the properties of these nanoparticles are identified.

Recent studies indicate that some effects are not completely benign to biological and environmental targets (16–21). Concerns regarding potential health risks and the environmental impact of engineered nanomaterials should prompt a proactive approach to ensure that the rapidly growing nanotechnology industry is environmentally benign and sustainable. Since fate and transport of nanomaterials under a variety of conditions have not been systematically studied, potential risks and hazards of nanomaterials in the environment will be addressed in a general way using the few examples that are available.

1.2.1 Exposure

Release of nanomaterials into the environment will most likely arise from several points in the nanomaterial “life cycle,” including release during the manufacturing process, use of products into which nanomaterials are incorporated, and, inevitably, with the disposal of these products. Yet, little is known about a nanomaterial’s fate and behavior in the environment. Mobility and interaction with biological systems largely depend on the specific size, shape, and chemistry of a nanomaterial. Thus, different types of nanomaterials will have different types of impacts on the environment and human health.

1.2.2 Fate and Transport

Unlike free particles, nanoparticles contained in a matrix are not considered dangerous. Nevertheless, products into which nanomaterials are incorporated will be expected to breakdown with time and to release nanomaterials in some form, possibly as free particles, into the environment. As with chemical compounds leaching from landfills, nanoparticles may also enter and travel through the natural environment, potentially in different ways than larger particles. Once in the environment, a number of factors may sequester, modify, mobilize, or degrade nanomaterials, thereby influencing their bioavailability and potential toxicity. Again, the fate and behavior of nanoparticles in the environment may not necessarily be predicted from what is known of chemically similar material at a larger scale.

One example that underscores the unique and unpredictable behavior of nanoparticles is that of fullerenes. It would be predicted that an all-carbon molecule, such as a fullerene, would be quite hydrophobic and insoluble in water. Interestingly, researchers have found the hydrophobic fullerene molecules acquire charge, forming clustered structures [nano- C_{60} (nC_{60})] suspended in water (22–27). Such suspensions would permit greater distribution of fullerenes in the aqueous environment. Additionally, while salt-free solutions solubilized the nC_{60} fullerene crystals (28), high salt conditions neutralized the nC_{60} fullerene crystals, causing them to fall out of solution (29, 30) and setting up the potential for their accumulation in sediments. These studies and others demonstrate that the fate of fullerenes can change depending upon the properties of the aquatic ecosystem in which they are found.

Indeed, a principal factor that will affect the environmental fate of nanomaterials is water solubility. Water solubility correlates with the potential for dispersion over vast areas and increases the potential for exposure. It is unknown whether nanomaterials with low water solubility will bind with organic molecules in the aquatic environment to increase their affinity for the aqueous phase and potentially increase exposure to biota. As discussed below, interactions with bacterial communities, mineral surfaces, and pH gradients are also likely to influence the fate and potential risks of water-soluble nanomaterials.

Water solubility of a nanomaterial is an important attribute for many applications. For these purposes, unique surface coatings and derivatives are being developed to deliver nanomaterials for *in situ* groundwater remediation and delivery of drugs. For

example, nanoiron is coated before being introduced into the environment for groundwater remediation (31, 32). Quantum dots consist of a metal complex core that is coated for biological activity (18). Hydroxylation of fullerenes increases their solubility (33) and permits their use in drug delivery and other therapeutic applications. The cytotoxicity of fullerenes derived for the purpose of water solubility was found to differ up to several orders of magnitude (34). Adding charged functional groups or surface coatings generally improves water solubility and suspension characteristics of nanoparticles. However, they can also impart selectivity in physical or chemical interactions, both with their intended targets and with indiscriminate entities in the natural environment. As a result, such modifications may influence the toxicological or ecotoxicological profile of a nanoparticle.

An additional factor that will affect the fate of nanomaterials in the environment is the ability to form large colloidal aggregates. Carbon nanotubes and nanoiron particles form aggregates of much larger dimensions than the individual nanosized particles (35–37). The large surface areas of smaller nanoparticles may allow for enhanced bioavailability and, consequently, greater potential for exposure and toxic effects. Evidence suggests that the adverse effects of fullerenes on bacterial populations are greater for smaller aggregates than for larger ones (38), and the antimicrobial properties of TiO₂ nanoparticles are inversely related to particle size (39). In contrast, the tendency of a nanomaterial to attach to surfaces or form aggregates can prevent its flow through porous media such as soil or reduce its bioavailability and exposure potential. Thus, factors that promote aggregation of nanomaterials in the environment can modify transport and subsequent toxicity. Depending on the specific nanomaterial, aggregation may mitigate both exposure and toxicity in some cases, while in others, it may increase the risk of toxic effects.

Apart from possibly being toxic in their own right, nanoparticles may provide surfaces that bind and transport toxic chemical pollutants. Possible nanoparticle association with naturally occurring compounds should be considered together with how this might affect their bioavailability and uptake into cells and organisms.

1.2.3 Transformation

Transformation of a nanoparticle in the environment will significantly influence its properties, including toxicity to living systems. Oxidation–reduction (redox) reactions are believed to be important for the transformation and environmental fate of nanomaterials. Chemical or biological oxidation is able to add, remove, or modify functional groups associated with mineral-based nanomaterials. Their high electron affinity and ability to participate in redox reactions (40) make fullerenes capable of producing reactive oxygen species (ROS) that can oxidize organic compounds in the environment and be key players in the induction and propagation of oxidative stress *in vivo*.

Microorganisms often mediate redox reactions in the environment. It is highly plausible that the interaction of nanomaterials with microorganisms normally present in soil and groundwater may alter nanomaterial transport, retention, bioavailability, and toxicological characteristics. Whether biotransformation of nanomaterials by microorganisms can occur to an appreciable extent in the natural environment and how

such transformations affect nanomaterial toxicity is unclear. The contribution of bacteria and fungi in soil and water to the degradation of manufactured nanomaterials needs further examination. Conversely, the effects of nanomaterials on microbial populations in the natural environment are also important to consideration. Microorganisms are a principal component of many ecosystems, serving as a basis of food webs and as important contributors to soil health. As such, disturbing microbial homeostasis would ultimately affect biota in all parts of the ecosystem. The ability of photoactivated TiO_2 nanoparticles to effectively oxidize organic matter and inactivate microbes (41–43) is not only highly useful for treatment of water systems but also presents a possible risk to natural microbial populations if discharged without regulation into the environment.

As seen with TiO_2 nanoparticles, UV radiation can also change the characteristics of nanomaterials (10, 44). Fullerenes strongly absorb UV light and in a manner similar to TiO_2 , photoexcitation can lead to the generation of cytotoxic reactive oxygen species (40). Quantum dots have been found to degrade under photolytic and oxidative conditions (18, 45), as occurs in the natural environment. Compromising the bioactive coat of quantum dots can expose the metalloid core, which is potentially toxic and may lead to undesirable or unanticipated reactions. Thus, chemodynamic reactions in the environment, such as photochemical changes and biodegradation, can contribute to the breakdown of nanomaterials.

In addition to the transformations that nanomaterials may undergo in the natural environment, it is also important to consider the ability of nanomaterials to affect elements with which they come in contact. TiO_2 and ZnO have long been used as fine powders in many sunscreens because of their ability to absorb or reflect UV radiation and reduce the amount of UV rays penetrating and damaging the deeper dermal layers of the skin. TiO_2 and ZnO have semiconductor and, consequently, photocatalytic activity that can promote the transformation of organic molecules upon absorption of radiation (46, 47). For this purpose, TiO_2 nanoparticles have been used to catalyze the photodegradation of environmental contaminants (48–50). A point of consideration may be the toxicity of TiO_2 -initiated photodegradative reactions and any resulting products in the environment. It also remains to be seen whether the UV absorptive qualities of TiO_2 have the potential to disrupt food chains by competing for the UV energy on which marine and freshwater phytoplankton are dependent.

In summary, environmental fate depends on the chemistry of the specific nanomaterial and can be further influenced by environmental conditions such as physical binding or chemical reactivity with other compounds, water solubility, aggregation, and oxidation–reduction reactions. Modifications will greatly influence the behavior of nanomaterials, including their interaction with fauna and flora, accumulation in biological systems, and toxicity.

1.3 NANOMATERIALS AND BIOLOGICAL SYSTEMS

Although hundreds of tons of nanoparticles are released through emissions into the environment annually, little is known of their interactions with biological systems.

Once exposure occurs, the biological fate of nanomaterials depends on the balance of four processes: absorption, distribution, metabolism, and excretion. To determine the risk of nanomaterials, information is needed for each of these processes. Some studies have been done, but more are needed. Below is a discussion of the biological fate of nanomaterials—what is known and areas needed to be further explored.

1.3.1 Exposure and Absorption

Exposure to nanomaterials can occur via dermal, gastrointestinal, or inhalation routes. While exposure will depend on a number of factors, such as how well nanomaterials are contained during manufacture, how widespread their use becomes, and if they are biodegradable or recoverable, the extent of absorption into the biological system depends on the chemical and physical properties of the nanomaterial.

Nanomaterials are incorporated into many consumer products that are meant to be applied to the skin. Whether a nanomaterial enters the body through the skin can depend upon whether the skin is injured, to what degree the skin is flexed (51), and to what degree the nanomaterial is lipid soluble. The latter may depend upon the surface coating or carrier of the nanomaterial. For example, studies are currently being done to optimize carriers of nanomaterials for topically applied medicine (51, 52). As mentioned above, current dermal exposure to nanomaterials occurs via sunscreen and cosmetics, such as by UV absorbing TiO_2 and ZnO . There have been no human clinical reports of toxicity from TiO_2 and ZnO , and these two nanomaterials have only been found toxic at very high doses in cell culture systems (53). However, quantum dots topically applied to intact skin at occupationally relevant doses were found to penetrate and localize within the dermis in a few hours, which is a concern for occupational settings (54). Synthesized ^{14}C -labeled C_{60} was also found to be taken up by human epidermal cells when administered as a fine aqueous suspension (55). The C_{60} rapidly accumulated in human cells, although it did not cause acute toxicity or affect the proliferation of human keratinocytes until relatively high doses were administered (55, 56). If nanomaterials contaminate the water, air, or soil, dermal exposure may become widespread for many organisms.

Gastrointestinal tract (GI) exposure may occur from the use of nanomaterial-containing cosmetics or drugs or as a result of the mucociliary escalator clearing nanomaterials from the respiratory tract (57). Animals may also ingest nanomaterials on their skin when grooming. Once in the GI tract, nanomaterials can be absorbed, although the extent of absorption depends upon particle size, with smaller particles crossing the GI tract more readily than larger particles (58). In fact, a challenge with designing nanomaterial drug delivery systems is that nanomaterials tend to aggregate in the gut, which increases their size and lowers their absorption (59). Chemical property also influences absorption; for example, ingested iridium nanomaterials are not taken up by the GI tract very well (60), but C_{60} fullerenes are readily absorbed (61) due to their hydrophobic nature. The extent to which nanomaterials can enter the food chain and whether they will bioaccumulate is unknown.

Besides dermal and GI tract exposure, there is the potential for inhalation of nanomaterials. This is a primary concern in industrial settings. Widespread inhalation

of nanomaterials may also occur if nanomaterials become airborne and enter the atmosphere. Due to their small size, nanomaterials can form light dusts that are easily distributed in the air, inhaled, and deposited in the lung. The size (single or aggregate) and shape of a nanomaterial help determine where it deposits within the lung. Because of the difficulty in conducting uniform, controlled inhalation experiments, many pulmonary studies of nanomaterials have been done via intratracheal instillation in which a fine dust of nanomaterials is placed in the trachea and the animal breathes the dust into the lung. Intratracheal instillation of nanotubes (62, 63), SiO₂ (64), and TiO₂ (65) has resulted in pulmonary inflammation, granulomas, and/or interstitial fibrosis. We do not know if breathing nanomaterials would result in acute toxicity in humans or whether toxicity would be latent, as occurs with asbestos. Even so, studies support the ability of TiO₂ to produce pulmonary inflammation in rodents (66, 67).

1.3.2 Distribution

It appears that once nanomaterials are absorbed into the biological system, they can distribute throughout the body. ¹⁴C-labeled C₆₀, after being intravenously injected into female Sprague–Dawley rats, was found to be rapidly cleared from the circulation and accumulated in the liver (56). The ¹⁴C-labeled C₆₀ persisted in the liver for 120 h following the i.v. administration, suggesting long-term accumulation in this organ. Quantum dots injected into the dermis translocate to the lymph nodes (68). Macrophages and dendritic cells in the lymph nodes may take up these particles (69, 70), leading to perturbation of the immune system. Self-protein interactions with particles may change their antigenicity, initiating autoimmune responses. Nanomaterial–protein complexes have also been used to facilitate antigen uptake by dendritic cells leading to enhanced immune response (71).

Due to the cardiovascular effects of ultrafine particles, it is probable that nanomaterials can distribute throughout the circulatory system (57, 72). When rats were gavaged with I¹²⁵-labeled polystyrene particles (50 nm), a small percentage of the particles were found 8 days later in the liver, spleen, blood, and bone marrow (58). Research has shown that nanoparticles, such as TiO₂, can leave the lungs of exposed animals and distribute to other organs (73). Within the lung, nanomaterials can be taken up by alveolar macrophages (74), enter epithelium (57) or interstitium (75), or translocate across the alveolar epithelium (76, 77). Once through the alveolar epithelium, gold nanoparticles were found in the pulmonary capillaries (76) and blood (73). Silica-coated magnetic nanoparticles containing rhodamine B isothiocyanate given intraperitoneally to mice were able to cross the blood–brain barrier and be found in the brain (78). Nanomaterials are known to enter the brains of monkeys, rats, and fish via the olfactory bulb (79–81).

Taken together, these studies demonstrate that nanomaterials can distribute within the cells and fluids of the body and translocate from organ to organ. Nonetheless, this translocation is highly variable and, again, dependent on particle size, surface characteristics, and chemical composition. The extent to which a nanomaterial enters into and translocates within the body will have a significant impact on human health.

There is currently an incomplete understanding of what forms of nanomaterials are bioavailable or whether they will bioaccumulate. It is too early to know whether nanoparticles applied on the skin, inhaled, or ingested can find their way to organ systems distal from the site of absorption or what concentrations they will obtain in these organs. As always, effects seen for cultured cells might not apply to the human body.

1.3.3 Metabolism

Metabolism is a salient component in the clearance of a compound from the body. Again, metabolism will be dependent on the characteristics and chemical composition for a particular nanoparticle. Usually, polycyclic aromatic compounds are metabolized by the cytochrome P450 system. However, as mentioned above, after ^{14}C -labeled C_{60} was intravenously injected into female Sprague–Dawley rats, it was found to rapidly accumulate in the liver (56). Evidence suggested that the relatively long-term accumulation of ^{14}C -labeled C_{60} in the liver may have been the result of the C_{60} not being oxidized, as normally occurs with polycyclic aromatics.

Once nanomaterials distribute and reach a target, results can be either beneficial, as for a drug, or toxic. Metabolism plays a major role. To date, the primary cause of nanomaterial-induced toxicity is thought to be the generation of reactive oxygen species (15, 57). Quantum dots (82), single-walled nanotubes (83–85), and fullerenes (16) are associated with oxidative stress and/or the production of ROS. For example, lipid peroxidation was found in the brains of largemouth bass exposed to fullerenes (84), and ROS production, lipid peroxidation, oxidative stress, and mitochondrial dysfunction were found after keratinocytes and bronchial epithelial cells were incubated with single-walled nanotubes (15). The shape of nanomaterials (leading to electron instability), as well as the presence of surface metals and/or redox-cycling organic chemicals, is thought to be instrumental in producing free radicals (86).

ROS is harmful because it can damage cell membranes (membrane lipid peroxidation), leading to permeability problems; cross-link and fragment proteins; and cause lesions in DNA. Ultimately, this can lead to cell death or, if the system is overwhelmed, death of the organism. For instance, the ability of both fullerenes (87) and TiO_2 (7) to generate ROS confers antimicrobial properties. While bacteria are limited in their ability to take up particles >5 nm, it has been speculated that they die from nanomaterial-induced oxidative stress caused by their cell membrane, which houses their electron transport/ATP energy generating system, interacting with nanomaterial-induced ROS (17).

Veronesi and colleagues used commercially available titania nanoparticles approximately 30 nm in size, which they added to cultures of mouse microglia (61). They found that the titania nanoparticles engulfed by microglia triggered the release of ROS in a prolonged manner. If this was to occur in a real-life exposure situation, the prolonged release of ROS could subject the brain to oxidative stress, a mechanism underlying some neurodegenerative diseases, such as Parkinson's and Alzheimer's. Biological systems do have oxidative defense systems that can combat ROS. Currently, it is unclear whether nanomaterials can produce enough protein/DNA damage to cause cancer and at what levels or time of exposure this may occur.

Fullerenes and other nanomaterials are often derivatized for compatibility with biological systems. This means they will interact with cellular membranes and may even be endocytosed. Redox-sensitive nanomaterials, such as fullerenes, could participate in oxidation reactions to damage the cell membrane and affect cell permeability and fluidity, leaving cells more susceptible to osmotic stress or hindering nutrient uptake, electron transport, and energy transduction.

1.3.4 Excretion

Only a few studies have reported clearance mechanisms. For example, 98% of ingested C₆₀ fullerenes was reported in feces of rats (57), and alveolar macrophages were found to phagocytize nanomaterials (88, 89). Surface chemistry and physical properties will influence to what extent nanomaterials are cleared from the body by urine/feces, dermis, hair, breast milk, and breath, or whether they will be sequestered in body tissue for many years. Ultimately, excretion influences the length of time that the body is exposed to nanomaterials and how nanomaterials are released into the environment.

In summary, there is evidence that nanomaterials can be absorbed, distributed, metabolized, and excreted by the biological system. At present, the scientific data from studies on ultrafine airborne particles are the best approximation available for potential health effects from exposure to nanoparticles. However, much more information is needed to adequately evaluate the biological toxicity of nanomaterials.

1.4 CONCLUSIONS AND DIRECTIONS FOR THE FUTURE

Whether or not applications for nanomaterials involve their direct introduction into the environment, as with the use of nanoiron in groundwater remediation and the widespread incorporation of nanomaterials into commercial products, it is clear that nanomaterials will eventually enter the environment. The great diversity of nanomaterials and types of applications, multiple potential points of release into the environment, and varied routes of exposure to populations make addressing the potential risks a complex task. Only recently have researchers begun to study the potential ecological risks and impacts of nanomaterial release into the environment (15, 88, 90, 91). To date, how much exposure to nanomaterials may adversely affect living organisms remains unknown, as do specific mechanisms of toxicity.

Rather than waiting for adverse effects or potential problems to appear before taking measures toward “damage control,” a precautionary approach with evaluation of risk to human health and implications for the environment may be conducted concurrently with the development of new nanomaterials. As long as the potential risks of nanomaterials are unclear, measures may be taken to ensure that nanomaterial release into the environment and exposure to the public is not left unchecked.

If nanomaterials prove harmful after being widely distributed in commerce, then the consequences will not be limited to only adverse health and environmental consequences. Expensive remediation efforts may ensue. A negative public perception of nanomaterials, as illustrated by the case of genetically modified organisms,

may thwart the many potential benefits nanotechnology can offer. Given the fact that there are suggestions that nanoparticles may affect human health and that commonly used sunscreens and many other products containing nanoparticles are on store shelves worldwide, consumers may demand labeling laws to inform the presence of nanoparticles in products.

There is a high level of uncertainty in terms of potential toxicity and latent, unforeseen impacts of nanomaterials in the environment. To appropriately address potential risks, better methods for the detection and quantification of nanomaterials in the workplace and environment (air, water, and soil) must be developed. Given that different types of nanomaterials will have different toxicological properties and types of impacts on human health and the environment, there is a need to establish a standardized set of criteria for assessing the most critical toxicological and ecotoxicological parameters and potential risks of nanomaterials on an individual basis. A standard of safety and suitable protective measures must be determined for those who are likely to be exposed to nanomaterials, especially in the occupational setting. Educational outreach services and information need to be made available to industrial hygienists, physicians, healthcare providers, veterinarians, and wildlife managers about possible exposure scenarios and proper precautionary measures to be taken to avoid undue exposure. Potential environmental, health, and safety concerns should be assessed early on in the researching and processing of manufactured nanomaterials. A system by which researchers and manufacturers may be encouraged to register, identify likely exposure scenarios, and provide at least a basic toxicological profile for their products should be established. Clearly, it is in the best interest of the public, regulatory agencies, and industry to integrate safety, toxicology, and environmental concerns into the research and manufacture of nanomaterials. Nanotechnology and its prospects should be promoted in a responsible and safe manner that acknowledges potential risks of nanomaterials being incorporated into widespread commercial production.

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