Nanoethics (2007) 1:47–56
DOI 10.1007/s11569-007-0003-x

ORIGINAL PAPER

Nanotoxicology and Ethical Conditions for Informed Consent

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Received: 22 February 2007 / Accepted: 22 February 2007 / Published online: 22 March 2007

Abstract While their strength, electrical, optical, or magnetic properties are expected to contribute a trillion dollars in global commerce before 2015, nanomaterials also appear to pose threats to human health and safety. Nanotoxicology is the study of these threats. Do nanomaterial benefits exceed their risks? Should all nanomaterials be regulated? Currently nanotoxicologists cannot help answer these questions because too little is known about nanomaterials, because their properties differ from those of bulk materials having the same chemical composition, and because they differ so widely in their applications. Instead, this paper answers a preliminary ethical question: What nanotech policies are likely to contribute to society's ability to give or withhold free informed consent to the potential risks associated with production and use of nanomaterials? This paper argues that at least four current policies appear to jeopardize the risk-disclosure condition that is required for informed consent. These are the funding problem, the conflict-of-interest problem, the labeling problem, and the extrapolation problem. Apart from future decisions on how to ethically make, use, and regulate nanomaterials, this paper argues that, at a minimum, these four policies must be modified. Government must spend greater monies on nanotoxicology; ensure independent nanotoxicology research; label consumer products containing nanomaterials; and avoid assuming that nanotoxicological properties are based merely on mass and chemical composition. Otherwise free informed consent to these new technologies and materials may be jeopardized.

Keywords Benefit · Conflict of interest · Consent · Disclosure · Extrapolation · Funding · Health · Labeling · Nanotoxicology · Policy · Risk · Regulation · Safety

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Introduction

People say the poison is in the dose. Today, however, the poison also is in the dimension.

At the level of the nanometer – one millionth of a millimeter – the properties of material things are very different. One reason is that, at the nanoscale, which is defined as 100 nm down to the size of atoms at 0.2 nm, quantum effects can begin to dominate. A second reason is that nanomaterials have a relatively greater surface area than do larger particles of the same mass of material. As a result, they are more chemically and biologically active, a fact that allows them to generate both great benefits and great risks (see, e.g., [20, 28]).

On the benefit side, many materials that are inert in their larger form become reactive when they are produced at the nanoscale level. This reactivity gives them important strength, electrical, optical, or magnetic properties. These properties, in turn, make nanomaterials important in hundreds of already-released commercial products, including anti-microbial wound dressings, catalysts, CD players, computer hard drives, cosmetics, fillers, LED-based traffic signals, low-friction coatings, microelectronics, opacifiers, semiconductors, and sunscreens. By the year 2012, US government estimates indicate that the nanotechnology industry will be worth $1 trillion [42], and its impact will be greater than that of the Industrial Revolution [28, p. 622].

On the negative side, nanomaterials' high surface reactivity and ability to cross cell membranes mean that they can be toxic to living things. About 1/80,000 the width of a human hair, nanoparticles have a small size that enables them to bypass through many of the body's protective mechanisms, like the blood-brain barrier [20]. As a result, some nanoparticles travel readily through the skin, into the bloodstream, throughout the body, and often deposit in organs like the brain. They penetrate cell membranes, lodge in mitochondria, and may trigger injuries such as oxidative stress, inflammation, protein denaturation, DNA damage, immune reactivity, and the formation of foreign-body granuloma responses [28]. For instance, once fullerene or buckyball nanoparticles (carbon particles having at least 60 carbon atoms) are in the blood, 90% of them are retained for at least a week, and after 1 week, nearly 80% of them can be found in the liver [29, p. 834]. Nanomaterials also have higher inflammatory potential, per given mass, than do larger particles having the same chemistry, and they may go undetected by the body's immune system. When nanoparticles are inhaled, the dominant pathway for human exposure [38, p. 36], their surface dimension or area is the "measurement that best predicts pulmonary toxicity" [28, p. 623]. The smaller they are, the more damage they can do. Scientists already know that nanoparticles generated under some occupational conditions can generate severe acute lung injury [29, p. 826]. Cadmium-selenium "quantum dot" nanoparticles have killed cultures of rat-liver cells [27], and water laced with buckyballs or fullerenes can damage the cell membranes of fish after only 48 hours' exposure [30]. To evaluate such problems, the discipline of nanotoxicology is emerging. It is the "safety evaluation of engineered nanostructures and nanodevices" [29, p. 823].

Ethical Debate

Because nanomaterials have both high potential for benefits and also apparent risks, public debate is emerging on whether their benefits outweigh their risks [5, 11, 15, 25, 40]. Under what circumstances is production of and exposure to nanomaterials ethically acceptable? This question is extremely important both because nanomaterials are already present in more than 320 consumer products [36, p. 2; 50], but also because companies like Mitsubishi in Japan have plants that annually produce tons of nanoparticles, like fullerenes, for uses in things like fuel cells and bowling-ball coatings [11]. Is such production and use ethical?

On the one hand, some groups are following the precautionary principle that regulatory action may be taken, based on the possibility of significant environmental or human harm, even before there is conclusive evidence of harm [18]. They believe that nanomaterials may constitute a whole new class of dangerous non-biodegradable pollutants. In 2003 the ETC group called for a global moratorium on the manufacture of nanomaterials until their interactions with living systems are better understood [17]. In 2004, the UK's Royal Society and Royal Academy of Engineering [38, p. 85] recommended "that ingredients in the form of nanoparticles undergo a full safety assessment by the relevant scientific advisory body before they are permitted for use in products." They also recommended that factories and laboratories treat nanomaterials as hazardous and thus reduce or remove them from waste streams [38, p. 8].

On the other hand, many industry-funded think tanks argue that nanotechnology and the many benefits it will bring through food, medicine, and energy technologies, will be slowed down by new regulations. Authors at the industry-funded Pacific Research Institute claim that nanotechnology needs no new regulations, but only self-regulation [6, 37]. Others, writing for the industry-funded Reason Institute, argue that the tremendous promise of nanotechnology will not be realized if people are driven by fear or seek zero risk; they also say that the risks of

stopping nanotechnology development are greater than those posed by the technology [7]. As a result, a number of scientists have argued that nano-related regulatory decisions are premature, because so little is known [29, p. 835]. Instead they say regulations should be based on scientific evidence of toxicity, especially toxicity of specific products and the likelihood of exposure risk [28, p. 627].

Who is right in the nanotechnology debate? At present, it seems difficult to say, for several reasons. As Nel et al. [28, p. 627] warned, "it is still too early to define what hazards and risks these materials may pose." A related problem is the lack of technical material on various nanotoxicological risks. Another problem is the great variety of nanomaterial uses. The applications of nanotechnology are very wide, some appear much risker than others, and there is great uncertainty about the outcomes of many of these uses. As a result, currently "governmental regulation is not possible, given the lack of needed information on which to base such regulation [29, p. 835]. Rather than simply opting for, or against, regulation, many scientists seem correct to argue for a tiered strategy, one beginning with testing (what appear to be) the more dangerous nanomaterials first [13, 29].

Conditions for Consent to Nanotoxicological Risks

In order to begin a defensible, tiered approach to eventual nanotech regulation, however, a number of ethical conditions must be met. These are necessary conditions for the possibility of making ethical decisions about risks associated with nanotechnology and nanotoxicology. Perhaps the key ethical concept related to risk and risk imposition is the notion of consent. Consent has long been the central concept in biomedical ethics, and it is the most crucial concept in all codes of ethics governing imposition of biomedical risks. Even democratic government relies most fundamentally on the consent of the governed. Hence a key ethical question about nanotechnology is whether current government policies are contributing to the conditions necessary to help citizens attain their rights to free informed consent to nano-related risks [19].

As developed in biomedical ethics, what are the classic conditions necessary to ensure free informed consent? According to traditional ethical theories, these conditions are disclosure, understanding, voluntariness, and competence. That is, the risk must be fully and clearly disclosed by those who want to impose it, its potential victims must understand it, they must voluntarily accept it, and they must be competent to give or withhold consent to it ([8], see [45, pp. 206–214; 44, pp. 17–20, 73–83, 105–113, 121–133, 164–175]). Citizens' rights to risk disclosure, the first of these four conditions, are often referred to as "rights to know" [4]. Rights to know guarantee that people can gain information about what might threaten them, such as societal production of toxic chemicals. While not sufficient to guarantee consent, risk disclosure and recognizing rights to know are ethically necessary in order to achieve informed consent. If one does know about some risks, because they have not been disclosed, then one cannot consent to them.

Consider first the condition of disclosure and its applications in the nanotechnology case. Have current nanotechnology policies provided conditions so that the associated risks and benefits of nanotechnology been disclosed to most people? In a 2006 US survey, 42% of Americans had never heard of the term "nanotechnology," and only 20% had some awareness of it. Yet, as the surveyors pointed out, older Americans and women, the people most likely to be using nano-containing consumer products, such as skin-care materials and cosmetics, were the least informed about nanotechnology [21].

If these survey results are correct, they indicate that most Americans have not received disclosure of nanotechnology risks. As a consequence, most contemporary people probably cannot give or withhold consent to the various risks associated with nanotechnology. As already mentioned, one reason that all nanotechnology risks cannot be disclosed is that experts themselves do not fully know or understand them. This means, in turn, that risk disclosure requires revealing to citizens both what is known about nanotechnology and nanotoxicology and what are the relevant uncertainties about them. Although many nanotechnological risks might be unknown, people could genuinely give or withhold consent to them, provided that risk disclosure included disclosure of all relevant unknowns and uncertainties.

What might help change this situation, in which most people using nanotechnology products or affected by them probably have not given genuine informed

consent to nanotoxicological risks? At least four conditions come to mind. (1) The government could adequately fund research on health and environmental impacts of nanotechnology. (2) It could ensure that most nanotoxicological research is not controlled only by those who are likely to profit from the technology. (3) Consumer products containing nanomaterials could be adequately labeled. (4) When assessing and regulating nanomaterials, government could avoid the assumption that nanomaterial properties can be known mainly through extrapolations based on their mass and chemical constituency. Unfortunately, however, none of the conditions (1) through (4) appear to be met in any governmental policies throughout the world. As a result, at least these four problems threaten citizens' free informed consent to nanotechnology risks. These can be called the funding problem, the conflict-of-interest problem, the labeling problem, and the extrapolation problem. Once these problems are addressed, both nanotechnology and ethical understanding of it are likely to progress.

The Funding Problem

Globally, governments annually fund nanotechnology research at just under $4 billion; in the US, annual government nanotechnology funding is about $1 billion total [42]. However, the funding problem is that too little government money is spent on nanotoxicology research, work on health effects of nanotoxins. Instead, most nano-related government money is devoted to developing new nanotechnology products.

Vincent Castranova, chief of a health-effects laboratory at the US National Institute for Occupational Safety and Health, says the federal government has devoted far too little money to studying the dangers of nanotechnology. El Clayton Teague, director of the US national nanotechnology-coordinating office, says the US federal government is spending about $10 million per year to assess health and environmental risks of nanotechnology, which is about 1 percent of the total annual federal nanotechnology expenditures of $1 billion. Other sources say US government nanotoxicoloogical research is just under 1% of this total government nanotechnology funding [14, p. 2]. Both government and top nanotoxicology scientists say they simply cannot test the needed nanomaterials with the few resources they have, and scientific publications bear this out. Thousands of scientific papers and patents tout different aspects of nanotechnology, but less than 50 address how the technology might affect people or the environment [13, 27]. Repeatedly scientists have called for additional government expenditures on nanotoxicology [24, 41]. The American Public Health Association (APHA), in particular, says that annual US nanotoxicology research should be approximately $100 million [2], or 10 times larger than it is at present.

If government-funded nanotoxicology is too minimal, research on ethical-social-legal aspects of nanotechnology is even more minimal. A Canadian group noted recently that there is a monumental increase in publications on nanotechnology, but not a concomitant increase in publications on ethical issues related to nanotechnology. Even when some scholarly activity is devoted to ethical issues associated with nanotechnology, ethicists say most of it is at the level of “generalizations and motherhood statements” [26, p. R10], rather than sophisticated analyses. They also note that because James Watson recommended that 3–5% of the international Human Genome Project be spent on ethical, social, and legal implications, this infusion of research funds energized the ethics community [26, p. R11]. Yet there are no comparably large sums of money to assess the ethical-social-legal aspects of nanotechnology, although the US National Science Foundation allocates a small amount to this specific area. Even the nanotoxicology necessary to ground ethical and social work is being only minimally funded.

These limited funds to investigate the health aspects of nanotechnology are especially problematic because what makes nanomaterials so promising is that their properties are radically different from those of the bulk forms of the same material. Yet these very differences are precisely why predicting nanotoxicological effects is both so difficult and yet so important (see [42]). Without adequate nanotoxicological research, the new miracle nanomaterials could turn into convicted killers or multi-million-dollar remediation headaches – like asbestos [42]. Thus it is illogical to tout the new properties of nanomaterials without, at the same time, recognizing the need for research on them. This lack of funding for health and ethical aspects of nanotechnology also is important because

"most sectors of nanotechnology are developing with no regulation" [11, p. 1166; 29]. Because of this lack of regulation, there is greater need for nanotoxicological research than in a more regulated industry. Also, because much nanotech funding (government funding) comes from members of the public, nanotech ought to be responsive to what members of the public want. If recent surveys in Europe are correct, the public is not so much worried about particular risks, like biotech or nanotech, but instead about the lax behavior of governmental and industrial institutions which, in the past, have failed to develop and regulate such technologies adequately [31, pp. 396–7]. If society does not fund adequate health and ethical-social-legal work on nanotechnology, especially work that addresses public concerns, dangerous products could be on the market without being tested adequately [27]. Even worse, public confidence in the new technology could spiral. As several Canadian bioethicists put it: "Either the ethics of NT [nanotechnology] will catch up, or the science will slow down" [26, p. R12].

The ethics of nanotechnology cannot catch up to the science, however, unless nanotechnology risks, especially nanotoxicology risks, are investigated and then disclosed to members of the public. Without such disclosure, citizens cannot give or withhold consent to nano-related risks. Part of such disclosure ought to include not merely scientific details but also the possible environmental-justice aspects of nanotech pollution burdens. (Environmental-justice problems are defined as those occurring as a result of unequal distribution of pollution-related, environmental-health risks, typically a distribution whose burdens fall heaviest on poor people, children, minorities, or workers [44]). Like many pollution burdens, those of nanotechnology appear to fall heaviest on children and on poor people. How does this occur?

Because the dominant route of exposure to nanomaterials is thought to be through the airways and into the lungs [38, p. 36], this exposure puts two groups in society at special risk, children and the ill. Toxicological research on airborne nanoparticles shows adverse respiratory and cardiovascular results, causing morbidity and mortality in the population. Particulate pollution, alone, causes 50,000 to 100,000 premature US deaths each year, especially among children, and engineered nanoparticulates could contribute to this problem. Even US consultants, hired by the Bush administration in 2000, admit the severity of particulate pollution. Although this administration has weakened air-pollution regulations and enforcement, its consultants admitted that airborne particulate pollution, alone, causes at least 30,000 annual, preventable US deaths [1]. A 2003 US National Cancer Institute (NCI) study drew even more disturbing conclusions. Studying more than half a million people over 16 years in 156 cities, it showed there is no safe level of air pollution, that exposure to fine-particulate pollution – like nanoparticles – is as risky as being overweight or exposed to cigarette smoke. Apart from cancer, effects of water and food pollution, or effects of other air pollutants like volatile organic compounds – the NCI study says each 10 micrograms of fine particulate pollution, alone, causes an 18% increase in heart-related deaths, an 8% increase in lung-related deaths, and a 4% increase in overall deaths ([32, 33], see also [47]), a disproportionate number of which occur among children.

Apart from effects of other air, water, and food pollutants, *Lancet* authors say that particulate air pollution, alone, annually causes 6.4% of children's deaths, ages 0–4, in developed nations. In Europe, this means that air particulates, alone, kill 14,000 toddlers each year [48]. These deaths occur mainly because, although many adults have defenses against premature disease and death caused by air, water, and other pollution, children often do not. Their developing organ systems, incomplete metabolic processes, and only partially developed detoxification systems are less able to withstand most toxins. Yet per unit of body mass, children take in more air, water, and food (and thus more pollutants) than do adults. Thus children are more likely to be harmed by pollutants, including nanopollutants, than are adults. The World Health Organization says that air pollution, alone, is associated with up to half of all childhood cancers [51, p. 155]. Children also could be especially at risk from nano-pollution-related neuro-developmental disorders because some airborne nanoparticles appear to concentrate nearly twice as much in the olfactory bulb as the lungs; this fact gives the particles access to the central nervous system and is consistent with studies showing air-pollutant effects on neurodegenerative disorders [20, 29, pp. 832–3].

Particulate air pollution, like that threatened by nanoparticle pollution, is also likely to harm the sick more than others, presenting yet another potential

environmental injustice from nanotechnology. Lung-deposition of airborne particles has been shown to be even greater among subjects with asthma and with chronic obstructive pulmonary disease [29, p. 825]. Even when nanomaterials are not airborne, there is some evidence that they harm the sick most. If nanomaterials enter through the skin, they often eventually make it to the circulatory system. Under certain disease conditions, like inflammation or some cancers, the endothelium (cells lining serous cavities, lymph vessels, and blood vessels) can become leaky and allow greater exit of nanomaterials and their accumulation in tissues [20, p. 308]. When nondegradable nanomaterials accumulate intercellularly, they either can stimulate free radical release, causing cell damage or inflamation, or can be taken up into the lysosomal compartment, where they can accumulate and cause toxicity or various diseases [20, p. 310]. While such accumulations may benefit those receiving nanomaterial drug delivery, they likely harm people already weakened by various disease conditions. Although different thicknesses of nanoparticle coatings can help determine whether they will accumulate in the lymph nodes (some thin coatings) or pass into the blood and then go to the liver (some thicker coatings), non-medical nanomaterials are unlikely to have these coatings. As a result, nanomaterials produced by atmospheric pollution or industrial processes are likely to accumulate in the spleen and liver [20, p. 310] – suggesting that the younger the people are at time of exposure, the more likely they are to be seriously harmed.

Although the preceding information, about how nanomaterials are able to harm children and the sick more than others, is preliminary, it is enough to suggest the need for more nanotoxicology research. More research, in turn, will provide a better information base, so that government can help educate citizens about nano-related risks, and so that citizens can give or withhold consent to various applications of nanotechnology.

The Conflict-of-interest Problem

Lack of nano-related risk disclosure, necessary for informed consent, is not merely threatened by inadequate government nanotoxicology funding. It also is threatened because much of the existing nanotoxicology research is done by those with conflicts of interest, those who stand to gain financially from use of various nanotechnologies. The conflict-of-interest problem is that "much of the information relating to the safety of these [nanomaterial] ingredients has been carried out by industry and is not published in the open scientific literature" [38, p. 5]. "Most sectors of nanotechnology are developing with no regulation and in an environmental ideally suited for entrepreneurship" [11, p. 1166] . Yet if much of the information related to nanomaterial safety is generated and controlled by those who stand to profit from it, then there is a basic threat from conflicts of interest, a threat that may jeopardize obtaining reliable information to be used for risk disclosure.

History clearly suggests that those with conflicts of interest may be less likely than others to reveal important health and safety problems with their products. That is one reason, after the famous Vioxx fraud and scandal, the American Public Health Association called for independent testing of pharmaceuticals, not merely relying on the chemical companies to test them. The APHA [3] warned that because the influence of industrial marketing activities on both consumers and prescribers is not balanced by independent evidence-based information, it was important to do independent testing and to expand independent assessment. Yet if independent testing is necessary for chemical-companies' pharmaceutical products, because of their conflicts of interest, independent testing is just as necessary for chemical-companies' nanomaterial products. The conflicts of interest are roughly the same in both cases.

Recall some of the past conflicts of interest that have made independent health and safety assessment necessary. In 1973, Conoco, BF Goodrich, Dow, Shell, Ethyl, Union Carbide, and other key companies who created the chemical revolution, were among those who signed a secrecy agreement to cover up studies, throughout the world, that showed dangerous health effects, including cancer, of even low-dose exposures to vinyl chloride. Moreover, they agreed to cover up these health effects even though the US National Institute for Occupational Safety and Health – NIOSH – officially asked for all health and safety information regarding vinyl chloride, and even though the industries themselves admitted that their failure

could be construed as evidence of an illegal conspiracy. As a result, vinyl-chloride standards were delayed for decades, and many workers died needlessly. Something similar happened with benzene. Although government scientists knew that it caused leukemia, the industry funded scientists to try to show that it was less harmful. For years industry medical officers denied benzene's toxicity. When the industry could no longer deny benzene's toxicity, it went to court, to stop the regulation, by arguing that the regulations to reduce benzene exposure would be too costly. As a result, benzene regulation was delayed for 10 years. Physicians at Mt. Sinai Medical School say that about 500 US workers needlessly died because of this delay. Likewise when Dow Chemical company discovered internal reports that its pesticide DBCP was a reproductive toxicant and could cause testicular atrophy, and when company scientists recommended exposure limits of 1 part per million, Dow covered up the reports, failed to reduce the exposure, and did not tell the truth. As a result, DBCP was kept on the market for at least 8 years after its harmful effects were known to company officials. Similarly, although the National Cancer Institute determined in 1980 that one phthalate, DEPH, caused cancer in animals, the Chemical Manufacturers' Association spent hundreds of thousands of dollars annually to thwart regulation. The same thing happened with many other chemicals. Because of all this coverup, lobbying, and political power, the chemical industry was able to stop all regulations proposed by the EPA under the first 5 years of the Toxic Substances Control Act, TSCA. Because of chemical-industry funding of opposition, no state right-to-know initiatives have passed since 1986 [9, 16, 34, 35, 43 ch. 2, 49].

Similar stories, of industry manipulation of science or manufacturers' coverup of research showing their products are harmful, have occurred repeatedly. Dow, Monsanto, and other companies covered up research showing the hazards of dioxin and chlorine compounds, then falsified their own research [9, pp. 141–160]. The chemical industry repeatedly funded misleading claims about the hazards of pesticides for children [16, pp. 153–173; 23, pp. 39–40; 49]. For years, the Ford Motor CompanyI produced its Pinto automobile, even though it new that it was prone to catch fire in rear-end collisions; the company failed to spend the $2.00 per vehicle to improve safety because it calculated that the cost of its payments to collision victims would be less than the cost of improving the car [10]. The tobacco industry likewise funded flawed research and, in the 1990s, even paid leading scientists hundreds of thousands of dollars to write letters and articles for influential medical journals, then later cited these letters and articles as if they were independent scientific work; in fact, many industries frequently pay scientists to sign their names to ghostwritten scientific articles that promote their products or mislead people about their risks [23, 35, pp. 199–201]. In more than one-third of all publications, researchers have shown that scientists publishing in biomedical journals have financial conflicts of interest regarding the topics on which they write, and that knowing the funders of studies often enables one to predict their conclusions [23]. In fact, there are a host of predetermined techniques for manipulating research protocols to produce studies whose conclusions fit the sponsor's predetermined conclusions; such techniques include short-term studies, so that toxic effects often do not have time to emerge [12, 16, 35, pp. 202–266; 43, ch. 3].

In the year 2000, when the independent Science Advisory Board of the US Environmental Protection Agency (EPA) studied all the product-related health and safety research of pesticide manufacturers, the members of the board did calculations of the studies' statistical power. They discovered that all the human studies "done by the pesticide manufacturers were scientifically invalid. They [the board] showed that to find a small effect, at least 2,500 subjects in each group were necessary. They also showed that the sample sizes used by the manufactures (7 to 50 subjects) to report no effect, had a 3–4% chance to find the effect" [39, p. C-1]. Thus the independent government committee showed that all of the chemical-industry pesticide studies were specifically designed to have small sample sizes. They were predetermined to generate false-negative conclusions, false conclusions that the pesticides were not harmful.

Because virtually all nanotechnology research is done by those who expect to profit from it, mostly chemical companies, there are few grounds for believing that this research, done with a clear conflict of interest, is likely to produce results that are any more reliable than the pesticide studies evaluated by the EPA Science Advisory Board in 2000. Thus it is unlikely that such "conflicted" studies could generate reliable conclusions about the health effects of

exposure to nanomaterials. To have ethically defensible nano-related policies, the government must rely on studies that are not tainted by conflicts of interest. After all, research ethics, especially health-related research ethics, has always stressed the importance of avoiding conflicts of interest [22, pp. 93–94, 224], as have all court systems. Yet for conclusions about nanotoxicology, the consequences of conflicted science could be even more damaging than the consequences of conflicted court rulings. The nanotoxicology case is an easy one in the sense that it provides merely an instance of a general rule that is well known in ethics. Moreover the rule to avoid conflicts of interest is one that ordinarily citizens appear to support for nanotechnology. In a 2006 survey only 12% of US respondents said that companies should be exclusively responsible for regulatory safety of nanomaterials. The vast majority of respondents wanted universities and the government to oversee nanomaterial safety [21].

The Labeling Problem

Citizen's rights to informed consent to various nano-related risks, however, are not threatened merely by lack of government health-related research or by conflicts of interest among those who do private nanotoxicology. Consent is also threatened when risk information is available but is not revealed to consumers. The labeling problem is that there are no requirements to label products that have nanomaterials, thus violating conditions for free informed consent and violating basic rights to know.

The American Public Health Association has long emphasized the importance of right-to-know provisions, especially concerning potential toxic threats. The APHA [4] recognizes that such rights to know are essential to informed consent, to preventing harm, and to treating conditions related to environmental exposures. The APHA emphasizes that rights to know are important not only to democracy but also to public health. Moreover, in the case of consumer products' containing nanomaterials, market requirements provide a second duty to guarantee appropriate labeling. By definition, efficient market exchanges and ethically defensible market exchanges require full information and free choice. Yet those buying products containing unlabeled nanomaterials have neither full information nor free choice. If not, then without labeling of products containing nanomaterials, even basic market requirements cannot be met. Purchasers have a right to know what they are buying. Labeling requirements for nanomaterials promote not only this right but consumers' giving or withholding informed consent to certain nanomaterials.

The Extrapolation Problem

The three previous problems indicate that certain government policies can thwart either obtaining reliable information about nanotoxicology or making that information available to consumers. Another threat to informed consent and relevant information-disclosure is the extrapolation problem, pointed out by Colvin [11], Cunningham [13], Monastersky [27], and others. This problem occurs when policymakers assume, as is done by many US regulators, that only the mass and chemical composition of nanoparticles, not also their surface area, is important to toxicology. As a result, they may set misleading safety regulations based only on mass and chemical composition. This is what occurred in 1999 when the US Food and Drug Administration ruled that for sunscreens, nanoparticles of titanium dioxide were not a new ingredient [11, p. 1167]. This extrapolation problem also occurs implicitly by virtue of the fact that US material safety data sheets (MSDS) for most nanomaterials list only properties and restrictions that are identical to those given for the bulk forms of the materials.

A more general extrapolation problem is that nanomaterials like carbon nanotubes and fullerenes are simply treated as variations of the underlying material, like graphite, an innocuous form of carbon, and thus are assumed not to require a new registration with the government. Yet these nano-level materials have very different properties from bulk forms of the same material [29, p. 835]. Because they also often have different toxicity per unit mass, different target areas, different exposure routes, and different dose-response curves, they require completely different risk assessments ([29, pp. 835–836). For instance, US government researchers showed that, when mice were exposed to nanotubes of graphite, at mass/dose levels comparable to what regulations allow for worker exposure to bulk graphite for 20 days, they developed lung scarring after only 7 days [46]. As a consequence

of nanomaterials' new properties, like these, it makes little sense to say that nanomaterials require no new registration or MSDS. Yet lack of new registration and new MSDS forms mean, as a consequence, that new nanotoxicological studies are discouraged; that there could be potential nanotoxicological problems in untested consumer products, that nanomaterial workers could be harmed; that consumers and workers are likely unaware of the risks they face by exposure to nanomaterials; and that, as a result, neither workers nor consumers can give or withhold legitimate informed consent. People cannot give legitimate consent to a risk that is misrepresented in the risk disclosure.

Where We Go from Here

If the previous arguments are correct, they suggest that the funding problem, the conflict-of-interest problem, the labeling problem, and the extrapolation problem all threaten the discovery of important nanotoxicological information. Yet this information needs to be disclosed as part of citizens' deciding to give or withhold informed consent to nanomaterial risks.

Both with respect to consent and with respect to their benefit-risk ratio, those who face decisions about medical applications of nanotechnologies are likely to be in a more desirable position than those who face decisions about non-medical applications. Because of testing requirements for new nanomedicines [29], it is likely that risk disclosure and therefore consent will be better satisfied for medical, than for non-medical, uses of nano materials. This is because the medical applications are likely to have access to more information that can be used for potential risk disclosure. Those who take advantage of medical, as opposed to non-medical, uses of nanotechnology are also likely to be benefitted because they can choose to avoid the nano-risks if they want, whereas victims of airborne nano-pollution often may not be able to choose to avoid the risks, especially if their exposure does not arise from a product they have purchased. Medical beneficiaries of nanotechnology also may receive the benefit of saving their lives, whereas non-medical beneficiaries of nanotechnology may receive lesser benefits. Thus the medical nanotechnologies, that are more likely to preserve rights to know and to informed consent, also may be more likely to have a higher benefit-risk ratio.

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