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SPECIAL FOCUS: GOVERNANCE OF NANOBIOTECHNOLOGY

Dynamic oversight: implementation gaps and challenges

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Abstract Nanotechnology is touted as a transformative technology in that it is predicted to improve many aspects of human life. There are hundreds of products in the market that utilize nanostructures in their design, such as composite materials made out of carbon or metal oxides. Potential risks to consumers, to the environment, and to workers from the most common passive nanomaterial—carbon nanotubes—are emerging through scientific research. Newer more active nanostructures—such as cancer therapies and targeted drug systems—are also increasing in use and are raising similar risk concerns. Governing the risks to workers is the subject of this commentary. The Occupational Safety and Health Act of 1970 grants the Occupational Safety and Health Administration the legal authority to set occupational health standards to insure that no worker suffers material impairment of health from work. However, setting a standard to protect workers from nanotechnology risks may occur some time in the future because the risks to workers have not been well characterized scientifically. Alternative risk governances—such as dynamic oversight through stakeholder partnerships, "soft law" approaches, and national adoption of international consensus standards—are evaluated in this article.

Keywords Benzene · Hard law approaches · International standards · Nanobiotechnology · Nanotoxicology · National Technology Transfer and Advancement Act · Occupational Safety and Health Act · Occupational safety and health standard · REACH · Soft law approaches · Governance

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Introduction

Nanotechnology is touted as a transformative technology, as it is predicted to improve many aspects of human life. It promises stronger and lighter materials, more efficacious pharmaceuticals, novel energy sources, more nutritious and longer-lasting foods, more sophisticated national security equipment, and revolutionary medical treatments. Government and large corporations have been the chief drivers of nanotechnology research and industrial commercialization. The global market for nanotechnology-enabled products in 2007 was worth $147 billion and is expected to increase to $3.1 trillion by 2015 (Lux Research 2007).

Several hundred products containing nanomaterials are already commercialized and in the marketplace (Project on Emerging Nanotechnologies (PEN)

2010). Most of these products can be classified as "passive" nanostructures chiefly made from carbon nanotubes. Passive nanostructures are often encapsulated in a solid matrix, such as composite materials, and, therefore, are characterized by relatively stable behavior. Bioengineering and nanotechnology have combined to produce more "active" nanostructures. This synergy has given rise to the new field of "nanobiotechnology," a field encompassing the applications and implications of active nanostructures interacting with living biological systems (Maynard 2009).

Specifically, "active" nanostructures are those that change or evolve during operation (National Science Foundation 2006). Examples of active nanostructure include applications such as cancer therapies, targeted drug systems, and cargo delivery systems (Afonin et al. 2010). Active nanostructures are more complex than passive nanostructures; they exhibit dynamic behavior and may pose greater risks to human health. As the second decade of the twenty-first century begins, more scientific publications involving active nanostructures have been noted (Subramanian et al. 2010). Applications of nanobiotechnology will undoubtedly represent a greater proportion of nanotechnology's developing economic portfolio in the second decade of the twenty-first century. Yet, despite nanobiotechnology's promise to transform many aspects of medical care, improving the range of disease outcomes, concern is growing that exposure to nanostructures—active or passive—may pose significant risk to human health.

This article addresses the question of how workers can be protected from the potential health risks of passive and active nanostructures when those risks may not be scientifically certain and when most occupational health experts believe that the current governance structures for protecting workers through government standards-setting (i.e., "hard law" approaches) are not robust (Choi and Ramachandran 2009). Despite the challenges facing traditional governmental occupational safety and health, total inaction is not appropriate—even if the face of uncertainty. Experience has shown failure to heed early risk warnings about new products or technologies can lead to adverse human health effects (Harremoës et al. 2001).

To prevent the adverse consequences that result from inattention to early signs of risk, risk governance is necessary even when scientific uncertainties remain (Davies 2009). Successful risk governance of nanotechnology—utilizing newer, non-traditional approaches—requires improvement in the scientific knowledge base, strengthening of risk management structures, promotion of stakeholder participation, and two-way communication among stakeholders (IRCG 2007). The challenges facing *occupational* risk governance are even greater given the limitations of the governmental occupational standards-setting process in the United States. (Howard and Murashov 2009). New approaches for ensuring dynamic oversight of nanotechnology and nanobiotechnology are needed and are under active consideration (Paradise et al. 2009a).

Nanotoxicology and occupational health risks

The vast majority of the investment in nanotechnology has been made to discover new applications of nanotechnology, and has not been aimed at elucidating nanotechnology risks to workers, consumers, or the environment (NRC 2008). This is not surprising. Looking back on the diffusion of new products and technologies in twentieth century commerce, it was often the case that the introduction of novel technologies occurred far ahead of the generation of knowledge about their risks. In the United States, commercialization occurs faster than studies of potential risks can be funded, faster than potential risks can be thoroughly researched, and faster than risk studies can be published and disseminated to policymakers for protective actions. Discovery and commercialization occur at a pace that far outstrips the development of protective risk-based standards that rely, in the United States, on well-developed quantitative risk assessment studies. In fact, the lag between commercialization and development of occupational health standards can often be measured in decades.

For instance, the most common nanomaterial that is used in passive nanostructures—carbon nanotubes (CNTs)—is a dazzling product from an applications perspective. CNTs have high tensile strength (100 times greater than iron), high electron mobility (1,000 times larger than conventional semiconductor materials), high electron emittance (100 times larger than conventional electron beam sources), high thermal conductivity

(several times higher than diamond), high hydrogen absorbability (five times higher than metals), and low density (half the density of aluminum) (Collins and Avouris 2000; Terrones 2003). Yet, knowledge about the potential health risks from exposure to CNTs is emerging slowly because of less-than-robust public and private sector funding. Researchers at the National Institute for Occupational Safety and Health (NIOSH) have begun to substantiate scientifically the concerns that risk prevention advocates (International Center for Technology Assessment (ICTA) 2008; Arnall 2003), insurers (Swiss Re 2004; Munich Re 2002), and scientists (Hansen et al. 2008) have expressed about the risk implications of nanotechnology (Shvedova et al. 2009).

Findings from the new field of nanotoxicology, based on previous scientific work that generated toxicity data on ultrafine particles in the nanometer range, suggest that some nanomaterials are hazardous and that uncontrolled occupational exposure to nanomaterials can lead to adverse health effects (Oberdörster et al. 2007). Specifically, NIOSH studies have shown that short-term inhalational exposure of single-walled CNTs in animals can cause inflammation, fibrosis, and granuloma formation at the level of 5 mg/m^3 (Shvedova et al. 2008). This level corresponds to Occupational Safety and Health Administration's (OSHA's) permissible exposure limit (PEL) for carbon graphite found in pencils—a relatively less harmful product. Other animal studies suggest that inhaled nanoscale titanium dioxide (TiO_2) could travel from the nose into the central nervous system and cause potential lesions in the brain (Wang et al. 2008). Yet, much is still to be learned about how nanoparticles migrate from a respiratory system point of entry to other organs of the body. These early laboratory findings only increase concern about the risks of nanomaterials, especially when coupled with data on nanomaterial emissions that indicate that exposures can occur in the workplace (Tsai et al. 2008; Peters et al. 2006; Kuhlbusch and Fissan 2006; Methner et al. 2007; Han et al. 2008). As the scientific literature on potential risks from nanotechnology increases, attention has focused on how to govern the risks to consumers, to the environment, and to workers. When workers need to be protected, the starting point for occupational risk governance is the Occupational Safety and Health Act of 1970 (OSHAct).

Limitations of governmental occupational health risk governance

In the United States, the OSHAct serves as the national framework for protecting workers from injury and illness at work. The OSHAct's purpose is to "assure so far as possible every working man and woman in the Nation safe and healthful working conditions" (29 U.S.C. § 651 2000). Congress granted to the secretary of labor the power to adopt mandatory occupational safety and health standards and to require employers to comply with those standards or risk civil and criminal penalties. Congress provided a broad delegation of authority to the secretary when it defined an occupational safety and health standard as "reasonably necessary and appropriate to provide safe or healthful employment and places of employment" (29 U.S.C. § 652(8) 2000). In adopting a standard that protects workers against toxic materials or harmful physical agents such as nanomaterials, Congress requires OSHA to set a standard "that most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity even if such an employee has regular exposure to the hazard … for the period of his working life" (29 U.S.C. § 667 2000). The legal authority to set occupational standards is clear in the OSHAct, but successful implementation of that authority has been less than successful (Lin 2007).

The heyday of occupational safety and health standards-setting for toxic materials (including carcinogens) occurred in the 1970s and early 1980s. The pace of standards-setting slowed considerably beginning in the 1980s. Although opinions differ as to the causes of the continued slow pace of OSHA standards-setting into the twenty-first century, one cause may be the increased complexity of standards-setting over time. The pace may have slowed due to regulatory requirements added by Congress, the President, and the courts to the process of developing and adopting an occupational health standard, especially the scientific support needed to pass legal muster, which is the availability of toxicity information. Of special legal significance in adding to the complexity of standards-setting is one particular court case—the U.S. Supreme Court's *Benzene* decision.

The OSHAct provides for judicial review of occupational safety and health standards. During OSHA's first decade, review by the courts of standards could be considered "deferential," but in the 1980s the courts began to scrutinize OSHA's standards more carefully. In its 1980 *Benzene* decision, the U.S. Supreme Court imposed a new threshold requirement for adopting an OSHA standard for a toxic agent. The Court said that before setting a standard, OSHA must determine if a workplace is unsafe "in the sense that significant risks are present" (*Industrial Union Department v. American Petroleum Institute* 1980). Since the *Benzene* decision, OSHA has had to perform a quantitative risk assessment to satisfy the legal requirement of demonstrating "significant risk" for every new toxic agent for which it intends to set a PEL. From a scientific perspective, this is a time and resource-intensive process. Determining when there is enough scientific evidence to satisfy the legal requirement for initiating standards-setting is not easy.

Even when OSHA wants to update an out-of-date PEL, the courts have laid down strict requirements that have stymied OSHA's progress in updating the PELs. In 1989, OSHA tried a more efficient approach to revising 212 obsolete PELs and establishing 162 new PELs by relying on occupational exposure limits proposed by NIOSH and private sector standards-setting entities. OSHA did not, however, establish significant risk for each chemical by conducting a detailed quantitative risk assessment (OSHA 1989). OSHA's "generic approach" was overruled by the Eleventh Circuit Court of Appeals because OSHA had failed to demonstrate separately that each PEL reduced a "significant risk" to worker health as required by the *Benzene* decision (AFL-CIO v. OSHA 1992).

In the ensuing two decades, various procedural and substantive requirements have been added to the Federal government's standards-setting process by Congress, the President, and the courts. By the mid-1990s, OSHA standards-setting was characterized as "ossified" by at least one commentator (McGarity 1992). In fact, OSHA's PELs (many based on science generated in the middle of the past century) for many toxic agents are considered obsolescent by most occupational safety and health professionals.

Beyond the legal challenges to the development of governmental nanotechnology standards for workers, the nature of nanotechnology itself presents a number of other challenges (Wilson 2006). Nanotechnology may refer to the manipulation of matter at the nanoscale, but the sheer number of nanomaterials (given that nanostructures can be developed from nearly all elements of the periodic table) and the various shapes of nanoscale materials (single-walled and multi-walled tubes, spheres, and others) present a challenge for substance-by-substance rulemaking (Howard and Murashov 2009). Grouping nanomaterials by similar molecular identity (e.g., carbon nanotubes, metal oxides, and metals), as the Organization for Economic Co-operation and Development has recommended (OECD 2008), may be more efficient. Even then, the challenges of standards-setting seem overwhelming. A program approach for nanomaterials has been offered as "more appropriate, including generic provisions relating to exposure assessment, risk controls, medical surveillance and worker training" (Howard and Murashov 2009).

The slow pace of OSHA standards-setting, and the unique challenges that nanotechnology presents, as well as other emerging technologies, have left many workers unprotected by governmental standards (McGarity and Shapiro 1993). This lack of protection is a part of the diminishing role of national and international occupational exposure limits in ensuring worker protection (Vincent 1998). For workers exposed to emerging technologies, such as nanobiotechnology, whose risks are not well characterized scientifically, reliance on OSHA occupational health standards-setting for protection in the near term seems misplaced.

Occupational health risk governance: alternatives

Industry involvement and stakeholder partnership

As policy makers struggle to overcome the challenges of developing regulatory oversight approaches for nanotechnologies, a number of alternatives have been offered to improve oversight based on a study of past oversight experiences (Paradise et al. 2009b).

One suggestion for improving oversight that would assist government in generating the data needed to satisfy legal requirements for standards-setting is for industry to take more responsibility for generating

toxicity data that can be used by government in determining acceptable risk (Murashov and Howard 2009). What's in it for industry—other than spending money on what could be done by the government, and historically, has been done by government? One answer might be that in joining in a partnership with other relevant stakeholders, industry would be a key player in developing consensus standards that government could use at a subsequent time as a foundation for mandatory standards. This would give industry a direct role—along with all other relevant parties—in fashioning downstream governmental standards that have had some "try-out" time.

In fact, a public–private national nanotechnology partnership has been proposed (Howard and Murashov 2009). Such a partnership of nanotechnology industry manufacturers and downstream users, workers, academic researchers, and safety and health practitioners would collaboratively develop nanotechnology risk assessment and risk control strategies. The consensus products of the partnership would provide an evidence base for consensus recommendations for occupational health standards aimed at eliminating or reducing worker risk from nanotechnology. In other words, the "significant risk" basis for occupational health standards-setting under the *Benzene* decision would be generated collaboratively.

Partnership, public–private consensus standards-setting, and subsequent industry-wide adherence to risk reduction strategies can also generate data about what implementation strategies work and do not work. Integrating these types of soft approaches to oversight with or following hard law approaches (such as mandatory standards with mandatory exposure levels) may be especially appropriate for nanotechnology oversight (Marchant et al. 2009b). Soft governance approaches may be more effective in a new industry than such approaches are in more mature industries with longstanding patterns of industrial practice. NIOSH has seen this attitude in its nanotechnology industry partnerships and has proposed utilizing these approaches in developing occupational exposure limits for nanomaterials (Schulte et al. 2010).

Hard law and soft law approaches

Hard law approaches—such as promulgating mandatory governmental standards when new risks emerge—have significant limitations, especially in the occupational safety and health area, as we have discussed above. Soft law approaches—such as international consensus standards-setting through a robust stakeholder process—can quickly achieve the consistency across national borders that international law takes decades to achieve. By developing international consensus standards and striving for substantial industry compliance at the earliest stage of commercialization, the usual "race to the bottom," where nations compete for jobs through lowering workplace safety standards, perhaps can be avoided (Haufler 2010).

However, one clear advantage that the hard law approach has in setting standards is in the diversity of stakeholders that are required by law to be a part of the process (Bell and Marrapese 2011). Regulators have the public interest clearly in mind when they develop standards. In contrast, consensus-driven voluntary occupational standards often arise from committees made up of technical experts only. It would be essential to the legitimacy of any privately developed occupational standard that worker interests are represented. In fact, the current value of most nanotechnology standards-setting entities lies in their technical expertise. To tackle the tough policy issues—such as the acceptable level of risk to workers—existing committees need to expand their representation beyond a technical membership to a broad-based, inclusive stakeholder membership.

In addition, robust external review of private consensus standards is also an important trait of the hard law approach to standards-setting. It needs to be equally robust in any voluntary consensus standards-setting process. Indeed, public review—not just expert review—is essential to the legitimacy of voluntary approaches to standards-setting, as risk perceptions can differ between technical experts and other stakeholders (Priest et al. 2010). If broad stakeholder representation and robust external review are a part of the soft law approaches to standards-setting, then soft law approaches may not be entirely different from hard law approaches. In fact, soft law approaches may be a valuable *precursor* to hard law approaches when the fund of scientific knowledge is too uncertain to permit regulatory standards to be adopted by law.

National adoption of international standards

In a global economy, the international harmonization of regulation may be beneficial (Marchant et al.

2009a). In addition to the incentives that a global economy provides to eliminate trade barriers, global economic competition may spur the development of consensus-based occupational health standards for nanotechnology. The exponential growth in nanotechnology in the years ahead could stymie even a well-funded and well-functioning national occupational safety and health standards-setting body, let alone one as in the United States that is challenged even by the task of updating its obsolescent PELs. Doing quantitative risk assessment for the toxic potential of all existing nanomaterials in the United States may take up to 50 years, with costs running into billions of dollars (Choi et al. 2009).

A more efficient approach to national standards-setting would be national adoption of international consensus standards—either in whole or in part. American "exceptionalism" may dampen official enthusiasm for such a gradualism to the traditional hard law approach, but manufacturers and exporters throughout the world already have to conform to several commercial and environmental standards in order to engage in business on a global scale. To have a greater voice in the development and application of international standards, Americans should engage more actively in setting international nanotechnology standards (Murashov and Howard 2008). Adaptation to compliance with international standards may increase as a result of the European Union's REACH regulation. REACH is an environmental health and safety regulation to which all manufacturers and importers who want to do business in the European Union (E.U.) must conform, at risk having their products excluded from the European Union (E.U.) (2006). REACH is unique in that past E.U. workplace regulations were directives that set minimum standards for performance, and each member state of the European Union was responsible for implementation through national laws. REACH is different in that it is truly an E.U. wide law; it is a *direct-acting* regulation, rather than requiring national implementation of its main provisions (Ogden 2010).

International standards-setting in the field of nanotechnology is quite active. International codes of conduct for nanotechnology, comprehensive risk management frameworks, technical guidance for manufacturers, nomenclature and metrology standards, environmental and consumer guidance, and guidance for occupational settings are being generated on a regular basis (Murashov and Howard 2010). Also, worldwide efforts aimed at developing occupational exposure limits for engineered nanomaterials are increasing (Schulte et al. 2010).

The field of nanotechnology may call for a new science-based, soft-hard law fusion approach to the governance of consumer, environmental, and occupational risk. If initial adherence to international consensus standards can be achieved, and those standards—after implementation experience is obtained—are followed by national "hard law" standards, then a new soft-hard law paradigm to standards-setting for emerging technologies may emerge.

In fact, the National Technology Transfer and Advancement Act of 1995 (NTTAAct) directs "federal agencies to focus upon increasing their use of [voluntary consensus] standards whenever possible" (P.L. 104-113 § 12(d)). Under the NTTAAct, Federal regulatory agencies are directed to use applicable voluntary consensus standards, except where their use is inconsistent with law or otherwise impractical. The underlying policy for utilizing already developed private standards is to save the government the cost of regulators "reinventing the wheel." The 2008 report by the U.S. National Institute for Standards and Technology (NIST) identified thousands of citations of standards incorporated by reference in procurement and regulatory documents (National Institute for Standards and Technology 2008).

Given the globalized flow of goods and services in the twenty-first century, one can imagine several benefits that can be obtained from this soft-hard law fusion approach. First, workers can be better protected against an emerging technology for which scientific uncertainty about risk persists. Second, industry benefits from settled standards that permit more stable commerce in nanotechnology and such standards insure a "level playing field" for global commerce. Third, multi-national employers can implement uniform risk management approaches regardless of country, achieving economies in environmental and occupational health and safety compliance. Fourth, government can more efficiently promulgate standards that have a good chance of achieving their purpose because they have been "road tested."

In a globalized world, the failure to achieve international consensus on standards can only impair

the commercial development of nanotechnology. Such failure would prolong thorough characterization of risks to consumers, the environment and to workers; delay nanotechnology's potential benefits for society; and risk harm to workers throughout the world.

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