
Science, Ethics, and the “Problems” of Governing Nanotechnologies

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That cacophony you hear is coming from the growing number of commentators addressing ethical, social, and policy issues raised by nanotechnology. Like many novel technologies that disturb the status quo, nanotechnologies raise questions about the adequacy of oversight systems; the extent to which the technologies push legal, moral, and political boundaries; and ultimately, the implications for human health and well-being. Because nanoscale techniques and products challenge our ways of thinking about biology, physics, and chemistry, nanotechnology forces us to reconsider accepted wisdom on toxicity, mutagenicity, contamination, biocompatibility, and other interactions among humans, the environment, and technologies. The sheer scale and reach of nanotechnologies demands institutions, collaborations, and conventions that can cross-link knowledge across organizations, disciplines, and locales. If ever there was an occasion to rethink the limits of disciplinary-specific knowledge, norms about regulatory processes, and societal implications of new technologies, nanotechnologies provide the opportunity.

This symposium presents historical case studies mapping development and oversight activities for a number of innovations with lessons germane to nanotechnologies.¹ The case studies do much to illuminate gaps in regulation and what worked or failed in developing oversight for novel products. The authors suggest approaching nanotechnology oversight by adding mechanisms to improve transparency and enhance cooperative collaborations, plus adding to scientific databases and risk assessment tools to deal with the uncertainties of nanotechnologies. While valuable in the short term, these measures may amount to little more than rearranging the deck chairs on an unstable ship without examining the value judgments and assumptions built into the technologies and systems around them. This paper undertakes such a task by examining some of the social, political, and economic values that have influenced regulatory infrastructures, taken-for-granted assumptions about safety and efficacy upon which evaluations have been based, and finally, exploring the role of bioethics and bioethicists in making policy decisions about novel technologies.

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Like the investigators in this volume, bioethicists and social commentators have also looked to the past to help them identify ethical problems and make sense of novel technologies. Unfortunately, many continue trying to fit ethical, social, and policy issues related to nanobiotechnologies into categories and analytical frameworks that may have fit older technologies and ways of thinking, but may no longer work.² There is a repertoire of moral concerns to which ethicists often resort in examining new technologies, which includes autonomy, protection of human subjects, access to expensive therapies, when life begins (retranslated in new techniques as when is something “alive”), and what it means to be human or to intervene in identity. Yet simply looking for precedents in order to understand the nature of a moral challenge and the degree to which it may be an actionable problem, or to compare ways that normative principles may apply, provides an impoverished analysis. Without taking into account the social and political contexts in which technologies arise, or the actual practices of direct and implicated participants, it is impossible to understand how certain conditions rise to the level of a moral challenge, much less to suggest a useful course of action.³ The histories of policy decisions and outcomes, situated within their relevant contexts, will not only provide better insights into future planning, but help to discern what (if anything) is unique to nanotechnology.

The histories of all medical technologies are intertwined with those of clinical and environmental medicine, health care delivery systems, national budgets and economic priorities, markets, and hierarchies of power. To illustrate, nanoviricides may provide new strategies for protection against infectious disease, yet cultural notions of contagion and traditional ways of thinking about containment within existing national and international public health bureaucracies may well influence how they will be used (or not).⁴ Existing tools to combat viruses are vaccines, which are expensive and time-consuming to develop, and are often ineffective for multiple strains and mutations. There is little incentive for manufacturers to produce or store them (much less develop new ones), since they are unlikely to be profitable. Because nanoviricides can be used in individuals after they are infected, the public health model could potentially shift from vaccination of large numbers of “at risk” populations (as well as traditional measures of quarantine or slaughter of suspect animal herds) to treatment upon infection. The role and responsibilities of public health professionals with respect to infections and pandemics might change as strategies shift from epidemiological surveillance (the historical basis for U.S. public health agencies) to point-of-care diagnostics in physicians’ offices.

Economic considerations are also key to policy decisions, however, not only in terms of the ability of companies to produce and profit from anti-virals, but also in terms of protecting international trade, tourism, or other sources of revenue dependent on the free flow of people and goods. An ethics of public health and policy is negotiated in the competing priorities of calming public anxieties, maintaining economies (especially for resource-poor countries), and protecting the public’s health — both domestically and internationally.⁵

At the same time, the history of vaccines (polio, pertussis, HIV-AIDS, human papilloma virus, and more) is rife with examples of scientific evidence taken into account in varying degrees vis-à-vis public concerns over safety (both safety from infection and safety from the vaccine product) as well as research and development costs. These cultural dynamics frame policy decisions, from definitions of risk, to funding priorities, to distribution and use. Questions include: Which vaccines should be mandatory? At what point does infection transmission become a social problem (i.e., switch categories from outbreak to pandemic, or go beyond what public health structures can handle?) Under what conditions should new technology alternatives be tried in the face of a pandemic threat?

The example of anti-virals demonstrates that there are collections of organizations, regulatory authorities, technology users and producers, and other relevant participants that should be taken into account. Such collectivities can be called a socio-technical network. Examining both the conditions and participants in such networks helps to illuminate the less-visible dynamics of governance, as well as the ways that values are embedded in technologies and institutions.

The project that produced this symposium will contribute to scholarly understanding about governance dynamics, in particular by asking whether nanotechnologies pose special risks or ethical concerns, and whether we may utilize existing regulatory schemes or must devise new ones. Through this paper I wish to highlight the idea that what gets identified as a problem (or not) says much about the socio-technical networks in which a technology operates. Understanding the dynamics involved requires going beyond traditional policy dissections and normative ethics models. Rather, we must examine governance in its broader sense in both informal and formal venues, as well as within historically specific and politically inflected forms.

In the sections that follow, I discuss the embeddedness of values in technologies and regulatory regimes, and raise challenges to usual understandings of risk that underlie existing regulatory systems. I end with a discussion of the role of bioethics in governance. The

paper is not meant to be comprehensive in covering governance needs. Rather, I focus on medical and biological applications of nanotechnology, and primarily at the preclinical and clinical evaluation stages, focusing on oversight in the United States.⁶ I invite policy makers, scientists, managers, ethicists, social scientists, legislators, and others to think in transdisciplinary ways, in order to communicate better about problem identification and resolution, as well as to apprehend the ethical, legal, and social issues that evolve with technological ones. That means not thinking of technology and its “impacts upon” society, but rather considering the ways in which each shapes the other.

I begin with a discussion of the Food and Drug Administration (FDA), the primary regulatory authority over medical products in the United States. Already challenged by a rapidly expanding range of responsibilities, strained resources, and limits on legal authority, the agency is being faced with products based on novel materials or science, with little knowledge about their possible effects. It is worth considering, then, whether the existing structures for decision making are sustainable for the future. Examining core elements of particular case histories of regulatory decision making is helpful in such considerations, but it is also important to bear in mind the political and social climates in which reviews were made. These environments arguably have as much effect on the evaluation of products as scientific assessment capabilities.

Regulatory Infrastructures

Socio-political environments may have subtle or dramatic effects on policy processes, but also may have long-term implications for decision-making infrastructures. A consumer-protection orientation from Congress or public concerns about a particular technology, for example, might encourage a more cautious, slower review process than an economic-stimulus orientation that might privilege innovation and getting products to consumers faster. Different orientations will affect socio-political framings of risk and benefit (e.g., what gets defined as a problem and hence, the degree of scrutiny and the means used for evaluation).

Such effects can be seen in the 1990s, the era of the “downsizing government” movement, in which federal agencies were scrutinized for what could be streamlined or outsourced. What was identified as a “problem” in regulating technology was excessive government (too many restrictions on innovation and too much federal spending on oversight agencies). Resources for the FDA were then constrained so that less intra-agency research was possible, product review was often handed over to third parties, and

other structural changes were made in order to speed products through review. Post-market review became a low priority, with few resources to conduct audits. Review times decreased, but within a few years very public disclosures of drug and device safety failures raised questions about the effects of streamlining on the public’s health.⁷ While the case studies presented in this volume begin earlier, it was during this period that governance changes affected evaluations for gene therapies, drugs, chemicals in the workplace, and agricultural products.

During the same period of time, medical products and therapies were becoming more complex. Tasked with assessing product safety and efficacy, the existing structures assigned medical products to oversight categories based on whether they fit the categorical definitions for drugs, devices, or biologicals. Yet products were increasingly hybrid in nature, using materials or delivery methods that could be defined as a drug/device (such as drug-eluting stents) or device/biologic (such as tissue-engineered skin), or that otherwise did not fit easily within the categories set up for drug, biologic, or device Centers. Now the “problem” facing technology regulation was ambiguity. Rather than tackling the underlying sources of uncertainty, an administrative patch was made. The Office of Combination Products (OCP), created in 2002 in the FDA User Fee and Modernization Act (FDUFMA, a product of the “downsizing government” movement), was intended simply to vet products and assign them to a Center for review based on their primary mode of action (PMOA).⁸ The vetting process quickly became more complicated than anticipated; not only were there many more combination products than originally anticipated, but determining mode of action is not straightforward with interactive, hybrid products.⁹ The OCP, conceived as an administrative patch to speed products through review and enable compliance with FDAMA, began taking on a different role, as interpretations of mode of action “made” a product into a drug, device, or biologic, each of which has its own distinct set of rules and procedures for evaluation. This was beyond the FDA’s formal role, which does not include opining about classifications of technologies or concepts of therapy, although by the FDA’s actions and decisions, the agency is in a sense doing just that.

Many medical therapies that will emerge in the next decade or so are also combination products, and this is certainly the case with nanobiotechnologies. The OCP estimates the growth of combination drugs to be 14% per year.¹⁰ Inter-center consultations increased 22% in 2006, and of these, there was an increase in consults involving all Centers, reflecting

the growing difficulty of distinguishing what kind of therapeutic object these new products are (and hence, which sort of risk and efficacy evaluations to apply). Based on this trend, it seems obvious (except perhaps to Congress and the FDA's Nanotechnology Task Force) that the system of product review based on early to mid-20th century discreet categories of drugs, devices, and biologics, and the available resource levels left from an era of downsizing government will no longer suffice.

Nevertheless, at the time of this writing, the FDA plans to continue regulating nano-products using categories set in the early 20th century. A special com-

mittee examining the issues concluded that no new regulatory scheme or category for review was needed.¹¹ Although they did recommend the development of additional tests and standards for specific measures of risk, these will continue to be category-specific for each of the Centers.¹²

Risk to human health and the environment is the most pressing issue in the governance of novel technologies, particularly when the effects are unknown. Yet the definition and measures of risk are challenged with nanotechnologies. As described in the previous section, the techniques and products are often combined with other technologies, making it difficult to categorize products by intended use, much less to tease out specific effects.

Proponents of using the regulatory status quo point out that many previously approved products contained particulates in the nanoscale range, and that many drugs go through a nanoscale phase in the normal course of being absorbed.¹³ They argue that generalizable principles can be used to evaluate products, no matter the method of manufacture or the mode of action. For example, it has been argued that smaller particle sizes should not be a cause for new regulatory schemes, since it has been shown that surface area per unit volume of particles can be a better measure than mass for assessing toxicity. Conventional mass-based dose measurements for drugs can be evaluated empirically before making conclusions regarding a nano-drug's potency or toxicity. However, for nanomaterials, surface area may be less important to biological interactions than surface modification, which many

manufacturers are using as a strategy to attract molecules, ferry molecules to specific sites, or deal with issues of adhesion. Such modifications would likely not be addressed under current provisions.

Rather than considering frameworks based on particle size or product category, an alternative might be to consider how the particles transform biological, chemical, or physical properties. These issues will increasingly come to the fore with the approaching wave of self-assembly and other techniques in synthetic biology, and with the marriage of nano to bio and informatics technologies, utilizing such complex techniques as self-assembly synthetic biology. Next-generation technologies have already emerged that will cause even more category confusion and uncertainties about what counts as relevant and acceptable evidence. The technologies themselves are moving targets. Simply pasting additional guidelines onto old frameworks may not be adequate.

The new problem, then, may be trying to lay transformational technologies onto old armature. The point is not to add a Center here or additional safety checks there, but to reconsider the infrastructure and logic by which products are reviewed. An example from another realm illustrates the potentially dire consequences of doing nothing. Alternative energy systems promise enormous benefits for reducing reliance on fossil fuels. But the existing infrastructure cannot handle energy produced in this way. There is no way to equalize surges or drops in production (with wind or sun variation, for example), nor is there any way to distribute energy at times and places where it is needed regionally. Power grids and transmission lines were designed around the most populous areas in the late 19th and early 20th centuries, and have not adjusted to the type and location of use today. Yet there has been no political will or funding to invest in new infrastructure. Rather, traditional energy systems have been patched with administrative duct tape. Laws are antiquated as well, with states having jurisdiction over some regulatory and distribution decisions and the federal government over others. So while plans for the future include a ten-fold increase in investment in the production of alternative energy technologies, they will fail no matter how beneficial or functional they are, without an appropriate system as a whole.

There are certainly pragmatic issues at hand: manufacturers need to know what regulatory pathway to follow, and with what specific kinds of data to demonstrate safety and efficacy. To change not only the forms of evidence but the logic behind the approval process, particularly midstream in the development of nano-products, could result in failure of potentially beneficial products and in extreme cases, the end of small, innovative firms. It is far easier to modify or add to existing guidelines than to rethink the logic and institutional forms that underlie product regulation, particularly in a time of limited resources, public criticism, and burgeoning demand for review. Yet this will not solve long-term problems of what constitutes relevant evidence of safety and efficacy in complex, combination products, what sort of expertise is required, and how to consider accountability to various publics.

Effective governance requires trust and credibility. By the first decade of the 21st century, stories began circulating about political interference (attempts to plant political appointees on advisory and review committees, unspoken mandates to review certain products favorably, instances of advisory panel warnings going unheeded). These concerns have led to decreased public confidence in the FDA's ability to conduct neutral, comprehensive reviews. The current climate has turned much more cautious, in light of problems from the past decade and highly visible, controversial treatments under consideration, such as stem cells. Also, efforts have shifted within the agency in response to publicly perceived needs to focus more on food safety and surveillance of international sources of supplies and manufacture. There was no permanent FDA Commissioner at the start of 2009, and morale of regulatory officials was suffering. And all of this is occurring during a time of unprecedented economic turmoil and lack of trust in oversight systems (for all aspects of life and work — financial, health care, and environmental).¹⁴ It remains to be seen which concerns will emerge as most important, and which kinds of technological, administrative, or other solutions will be applied.

Regulatory Responsibilities: Interpretations of Safety and Efficacy

Risk to human health and the environment is the most pressing issue in the governance of novel technologies, particularly when the effects are unknown. Yet the definition and measures of risk are challenged with nanotechnologies. As described in the previous sec-

tion, the techniques and products are often combined with other technologies, making it difficult to categorize products by intended use, much less to tease out specific effects. Interactions between components of a technology at the nanoscale or between nanomaterials and human tissue may not be linear, and most testing logics reduce interactions to single-outcome measurements. Predictive algorithms may also be questionable, as many nano-techniques rely on the ability of materials to behave differently at the nanoscale than at larger, more familiar scales.

What has been less considered are the fundamental understandings of human biology and lived environments upon which such models of effects and predictive measures of outcomes build. To take one example, the classical concept of biocompatibility gauges

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responses of the body to foreign substances in terms of inflammatory, immune, mutagenic, or thrombogenic reactions.¹⁵ This assumes there is a defined “self” that needs protection from an “other.” In regenerative medicine, however, bioactive substances are meant to be *interactive* with and eventually indistinguishable from native tissue, utilizing the body's own mechanisms to build new tissue, send signals to initiate hormone or enzyme cascades, or otherwise restore function. Indeed, inflammation (conventionally viewed as indicating incompatibility) is now thought to be beneficial in some forms of tissue regeneration.¹⁶ Another example comes from traditional device-based views of risk, in which measures of biocompatibility commonly focus on surface characteristics of the device or other features that may cause a host reaction. However, with proposed nanobiosensors or other indwelling nanodevices, other forms of compatibility will have to be considered, including mechano-biocompatibility. Specifically, mechanical forces from vibration, tugging, or locomotion of nanoscale devices can modulate cell function, disrupt cell signaling, or activate metabolic pathways in cells.¹⁷

Such new understandings of interactions within the body will be key to reconsidering what constitutes risk. Certainly there are known potential problems with tiny particles causing agglutination or migrat-

ing to tissues in an uncontrolled fashion as well as unknowns that will require further study. At a deeper level, however, accepted knowledge about the relation of bodies and technologies, as well as indicators of harm, may no longer be valid. With such intimate symbiosis, we may have to rethink cultural notions of “foreign” substances, purity, containment, and crossing bodily boundaries.

In next-generation techniques, molecules may self-assemble, and DNA may be synthesized to create minimal genomes or organisms that do not exist in nature. Synthetic biology may allow us to change the basic “operating system” of biology (nucleic acids and amino acids), creating systems in which the codons that instruct cell mechanisms to make particular substances can be directed to function in new ways, or the number of amino acids required to assemble proteins — the basic materials needed to make life “work” — can be altered.¹⁸ In what sense can the “efficacy” of such technology be evaluated? What sort of product review conventions and risk definitions could deal with creating new life forms and potential changes in evolutionary processes? Who should make these value judgments?

The point is that these are conceptual issues that will require more than just coming up with a new metric or agreement about safe levels of toxins or emissions. The 2007 FDA report on nanotechnologies, however, focuses on the adequacy of testing approaches rather than addressing the assumptions that underlie definitions of risk.¹⁹ The report recommends making adjustments and additions to protocols (for example, because nano-drugs differ from larger particles in their pharmacokinetics). New tests, metrics, and instruments can be devised to test any set of products with novel characteristics; additional standards or threshold limits can be established. However, the concept of risk is about more than the interpretation of scientific facts produced in this way. Rather, risk has a social dimension, and there are values embedded in the way particular that hazards are identified as being risks in need of containment.²⁰ Evaluation of risks and decisions about mitigation are shaped by the participants involved.²¹ This includes those in regulatory agencies, but also politicians, public or lobbying groups, insurers, technology assessment advisors, and users. All participate in the identification of certain kinds of things as risky and in assigning relative importance to the risks.

The Role of Bioethics

I have given a few examples of how judgments, interpretations, and values suffuse regulatory structures and practice, affecting what gets defined as a “prob-

lem,” what comes to count as acceptable evidence, and how decisions are made about individual products and product types. If values and moral judgments are implicitly a part of governance, should ethics and social science be explicitly a part of deliberations about research, product development, or policy directions?

Historical case studies of biotechnologies would be improved by including the accompanying history of bioethics and its role in medical science and technology innovations. Bioethics as a field arose from growing awareness of abuses in both clinical and research settings in the mid-20th century, and thus has been rooted in reflections on the physician-patient relationship and concerns for protection of human subjects in research. This focus on the individual, often framed in terms of rights and entitlements, remains important, and explains ongoing concern about consent, access and cost, and whether certain kinds of products may create unfair advantages for some. By the 1970s, with the rapid growth of medical technologies that challenged concepts of life, death, and “therapy,” and with strained health care resources, the questions began to shift. Bioethicists became more directly involved in contributing to policy debates, and the field was institutionalized in the form of commissions, advisory councils, and expert testimony. The utilitarian framework used by a number of bioethicists evaluated new technologies in terms of risk or benefit, and thus aligned with parallel deliberations in regulatory arenas. This frame focuses attention more on the population than the individual. Ethicists such as Jonathan Moreno have cautioned that thinking of the ethical issues in terms of risk, focusing on quantified and assigned threshold levels that are applied at population levels may go too far in the direction of eliminating consideration of individual conditions.²²

Over time, individuals and groups not typically associated with ethics expertise have taken up the language of bioethics to promote their own positions, which may be related to either political, economic, or consumer interests. Prominent examples include the debates over genetically modified organisms and stem cell research, in which environmentalists, consumer rights groups, religious organizations, anti-abortion activists, public intellectuals, and others have questioned the goals, values, and presumptions that get built into science and technologies. Patients and disease proponents are going beyond advocacy and lobbying roles, directly participating in policy decisions about access to treatments and even the design of clinical trials. In the process, the focus of deliberation has shifted somewhat from safety and availability arguments to moral arguments. As exemplified in debates over reproductive technologies and most recently,

stem cell research, bioethics perhaps more than any other field has become highly polarized — not only in terms of analytical standpoints, but rather in terms of right and left politics, and those who enthusiastically support or fearfully oppose social and technological changes. Bioethicists and others commenting on nanotechnologies are no exception. Yet framing nanotechnology as a utopian dream or apocalyptic nightmare and utilizing fantastical scenarios as the basis for analysis does little for sound ethical reasoning (and does even less for the credibility of bioethicists).²³

It is axiomatic that decisions about new technologies do not exist in a vacuum. The context for policy making includes more than institutional infrastructures or deliberations over using old or new methods for assessing risk and benefit.

The uptake of ethics outside of traditional arenas has raised questions for many about the proper role of bioethics. Some might argue that legislators and regulators have assimilated ethics justifications to execute policy priorities. Others ask if bioethics should create a space for deliberation about values in choosing and deploying technologies, particularly when such discussions are excluded from regulatory deliberation. Should such a space be external or internal to the process of deciding public policy? Opinion is divided about whether moral values should be made an explicit part of assessing new technologies.²⁴ Here we can learn from past examples of reproductive, life-extension, and genetic technologies.²⁵ Alta Charo sounds the alarm about the degree to which ethics has become politicized, particularly since the late 20th century. She sees dire implications for public policy when individuals with specific worldviews and agendas are placed in positions of quasi-authority to make decisions.²⁶ Charo is committed to an ethics of the polity, but is cautious about state regulation of morals. She calls for a public bioethics as the basis for public policy formation, a bioethics that looks towards the good society, rather than one overly focused on individual choices.

What then is the proper relationship of bioethics to the law, including law establishing regulatory policy and review? Susan Wolf points out that while ethicists have thought of law as providing protections for rights

and liberties, profound ethical and policy questions are raised when the law is used by official ethics commissions to create prohibitions and enforcements that may come from ideology rather than careful, inclusive deliberation. Using the example of the President's Council on Bioethics' attempts to ban or constrain certain technologies, she argues that law must be used responsibly to pursue ethical goals.²⁷

The history of medicine, policy, and ethics taken together shows how a sense of obligations may change over time and as differing forms of expertise are included or excluded from sociotechnical networks. History also shows how social anxieties are expressed through reactions to technologies. I would argue that the current obsessions with nanotechnology's effect on privacy and with the use of nanotechnology for enhancement, for example, are more likely about deep cultural concerns (North American, anyway) about loss of personal control and the blurring of boundaries between individuals and the state or other authorities, than about the actual use of nanochips to relay information or to stimulate neural pathways.

Given this, policy becomes a tangible expression of the hopes and fears of a society. The cultural work of dealing with ambiguity is channeled into crafting regulations, ethical guidelines, standards, metrics, and predictive algorithms, all of which are socially negotiated attempts to deal with indeterminacy.

Toward Alternative Forms of Governance

The relative roles of bioethics, social scientists, policy experts, scientists, managers, governmental authorities, and ultimate users of technology are still in flux. The addition of new participants such as advocacy groups, protestors, various official and non-official ethics advisory groups, "citizen scientists," and others is an indicator that many people have little faith in existing systems of governance. What is clear is that transformative technologies call for transformative thinking about governance.

It is axiomatic that decisions about new technologies do not exist in a vacuum. The context for policy making includes more than institutional infrastructures or deliberations over using old or new methods for assessing risk and benefit. Rather, the dynamics of particular socio-technical networks may influence what gets defined as a technological or social problem and what approaches are taken to those problems. Social and economic environments are not static. Ideas about what constitutes the social good, what social and health needs should be prioritized, and who is respon-

sible for what kinds of decisions, change over time and circumstances. In North America, for example, trends toward personalized medicine, evidence-based medicine, and individual responsibility for health say much about the neoliberal economy in which policy is being made.

Regulatory review of products must not only recognize historical and social locations, but must be better linked to both upstream and downstream arenas of activity. Nanotechnologies are repositories of human judgments. They embed values by favoring or facilitating certain ideas, while bypassing or undermining others. Upstream, researchers and managers must take seriously their responsibility to consider the health and social needs of societies, before being romanced by a technique or potential product capability. Downstream, clinicians and patients must bear in mind that policy decisions about new technologies must be made with respect to existing or alternative treatments that may provide cost, safety, access, or other benefits to society as a whole, and these concerns may outweigh their particular needs and desires.

Would scarce resources be better spent on less costly alternatives? Are the goals of particular research directions “worth it”? Bert Gordijn asks, and what, as well as whose, criteria should be used to make this determination? Are those goals actually achievable through nanotechnologies?²⁸ Beyond specific products, nanoscience and technologies will stimulate new knowledge about engineering principles, human biology, the development of disorders and responses to conditions, adaptability and evolutionary capabilities of humans, and more. This is not an insignificant contribution. In fact, working across disciplinary domains and assumptions will lead to new conceptualizations of problems, which may have a far greater payoff than a specific diagnostic technique, a real-time body-monitoring function, or even therapy.²⁹ Who gets to decide such things, should valuation be a part of formal oversight, and at what stage should this occur — product concept, regulatory review, or post-market use?

These are old debates about authority, jurisdiction, and expertise. Science, policy, and governance have all become hyper-specialized. Even within the study of risk, there are experts with differing skills and knowledge based in risk assessment, risk management, and prediction. Likewise, there are many kinds of technology assessment, with differing functions and priorities. While regulatory agencies scrutinize safety and efficacy, technology assessment organizations look at bigger-picture questions of alternatives, capacities, what value is added, and for whom.

If assumptions about underlying processes should be revisited, so should ways of working. While “inter-

disciplinarity” has become the catchword for fundable programs and organizations attempting change, nanotechnology may present the opportunity to take it seriously, both in research and governance. Experts in epidemiology, toxicology, physical and life sciences, as well as behavioral sciences rarely speak to each other. In an era of “omics” sciences (e.g., genomics, proteomics, metabolomics, etc.), knowledge of interactions at subcellular, inter-cellular, organismal, and organism/environment levels is producing fundamentally different ways of thinking about how systems work. Perhaps oversight policy should borrow a page from this multiplex way of thinking and working. If so, interdisciplinarity must become more than borrowing terminology and methods from other disciplines. Rather, it should become a more expansive way of considering thorny problems raised by emerging, high-risk technologies. Social, ethical, and legal expertise will also be needed for comprehensive understanding of the issues involved.

While some observers worry about bioethicists, social scientists, and others who analyze ethical and social issues being co-opted by for-profit entities or state interests, I worry more about the dangers of *not* engaging at all stages of technology and product development. Making after-the-fact judgments about therapies without communicating with those who designed them or without a sufficient understanding of the science is simply uninformed analysis. Circulating fantastical scenarios without knowing what is realistic can cause misplaced public concerns. While product manufacturers have traditionally resisted discussing ideas in the concept stage to avoid public misunderstanding and tipping off competitors, organizational practice is undergoing as much innovation as technologies. More organizations and researchers are beginning to work in open source, networked, and collaborative ways, as exemplified by the BioBricks Foundation.³⁰ The culture of closed boundaries and minds is changing. Manufacturers and researchers who recognize the value of transparency and need to communicate with ethicists, policy makers, and various publics early have benefited, through better product design and execution.

Downstream, new technologies have to meet the real-world demands of clinical settings, including the needs of both patients and clinicians. Innovations also have to confront evidence-based medicine, which has its own criteria for proof. Further, concepts of risk and its evaluation may differ in the domains of product review and pre-development technology assessment rather than in evaluation of products for actual use; standards of evidence and approaches to data analysis used by purchasers and those assessing usability in real

clinical environments utilize quite different criteria for risk, efficacy, and benefit. For example, nanoparticle vectors that dissolve after gene insertion or nano wound sealing agents will likely have considerable utility in the clinic, be safer than existing techniques, and may reduce costs, leading to positive assessments by clinicians and payers alike. Nanosurgical tweezers (touted as a technique for moving DNA bits), however, may more appropriately remain a (costly) lab tool rather than a practical application for clinical therapies.³¹ Then there is the level of everyday practice with patients. Would physicians' offices be able to handle the volume of information from 24-hour real-time data outputs from patients' indwelling nanobiosensors? With strained resources and lack of trained personnel, who will store, interpret, and analyze those data, much less take clinical action? These are common-sense issues that are rarely addressed in assessments of risk, benefit and efficacy.

There are many options for reformulating governance, including a number of informal and formal activities that serve to regulate behaviors, practices, and understandings of medical and scientific technologies.³² As Charles Rosenberg has stated, the work of making policy is contingent on options available within historical, social, and political environments: "Policy formulations and subsequent implementation provide us with opportunities to see the relevant costs and benefits as perceived by particular men and women as they choose among a variety of available options at particular moments in time."³³ Nanotechnology presents an opportunity to think in new ways about complex problems, to challenge the conventional knowledge and structure of regulation, and to consider the ethics of governance.

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2. Privacy (can sensing/tracking tools also be used for unwarranted surveillance of individuals?), and enhancement (do nano-enabled muscle fibers provide an unfair advantage to the elite?) are two items at the top of the nano worry list for many ethicists, but these properties characterize many old and new technologies, not just nanotechnologies. In an era of electronic financial transactions and data transfers, national security regimes that trump rights of private citizens, radio frequency identification (RFID) tracking devices on cell phones and ID cards, and electronic medical records, the meaning of privacy has changed. In American culture, authorities must be seen as protecting the privacy of individuals, so there is a theater of legislative activity, but privacy, in the sense of having control and choice over information dissemination as some philosophers seem to imagine it, no longer exists in law or social life. There is also a plethora of literature on enhancement technologies that has arisen in the past decade, attempting to distinguish enhancements from therapies and "normal" from post-human capabilities. I would argue that the reason for attention to these areas lies in underlying cultural concerns about control and fairness. Some commentators question whether there is anything ethically unique to nanotechnology at all. See, e.g., A. Grunwald, "Nanotechnology: A New Field of Ethical Inquiry?" *Science and Engineering Ethics* 11, no. 2 (2005): 197-201; M. Godman, "But Is It Unique to Nanotechnology?" *Science and Engineering Ethics* 14, no. 3 (2008): 391-403.
3. A few examples of the abundant literature on nanoethics now available include D. Evans, "Ethics, Nanotechnology and Health," in H. ten Have, ed., *Nanotechnologies: Ethics and Politics* (Paris: UNESCO Publishing, 2007); K. Kjølberg and F. Wickson, "Social and Ethical Interactions with Nano: Mapping the Early Literature," *Nanoethics* 1, no. 1 (2007): 89-104; and M. C. Roco and W. S. Bainbridge, eds., *Societal Implications of Nanoscience and Nanotechnology* (Boston: Kluwer Academic Publishers, 2001). Works that focus on autonomy, human dignity, and informed consent (i.e., primarily effects on individuals) include R. Brownsword, "Regulating Nanomedicine: The Smallest of Our Concerns," *Nanoethics* 2, no. 1 (2008): 73-86; and K. S. Shrader-Frechette, "Nanotoxicology and Ethical Conditions for Informed Consent," *Nanoethics* 1, no. 1 (2007): 47-56. Some aspects or applications of nanotechnologies may indeed recall long-standing concerns, but nanotechnologies are just not the same in terms of context or content as in vitro fertilization (IVF), genetic testing, or cognitive enhancement drugs, as some writers seem to suggest.
4. In contrast to existing drugs that target the influenza virus after it has already replicated inside human cells, nanoviricides target viruses in the bloodstream, before they infect cells. Hence, there is no need for the production of antibodies that vaccines would provide, and viral mutations are no longer significant. See N. Porter and L. F. Hogle, "Nanotechnology and Public Health: Redefining Risk and Containment," manuscript in preparation.
5. In the case of HPAI (avian flu) outbreaks, U.S. public health authorities focused on preventing transmission in humans. In resource-poor countries such as Viet Nam, where poultry raising is a primary industry, public health authorities wanted to control the virus in animals instead. Conflict arose as different intervention strategies - including technologies and the systems through which to deploy them - seemed to address very distinct social, political, and economic needs in addition to health needs. *Id.*, at 5. For more on vaccine policy dynamics, see J. Heller, *The Vaccine Narrative* (Nashville, TN: Vanderbilt University Press, 2008).
6. The unique properties of materials at the nanoscale are detailed in other papers in this symposium and will not be repeated here. The central question has to do with the fact that

- materials act entirely differently at the nanoscale than at the macro-level, as nano-particles can move across the blood-brain barrier, into the respiratory tract, and across cell walls. This leads many to question the individual and cumulative effects of various nanotechnologies on plants, animals, and the environment. Description of nanomedicine applications can be found in K. K. Jain, *The Handbook of Nanomedicine* (Totowa, NJ: Humana Press, 2008).
7. P. Hilts, *Protecting America's Health: The FDA, Business and One Hundred Years of Regulation* (New York: Alfred Knopf, 2003).
 8. Does the product act like a device (providing, for example, structural support or mechanical action), or a drug (acting as a chemical agent, with targeted effects specific to a molecule), or a biologic (a serum, vaccine, or blood component)?
 9. Many such hybrids had ambiguous modes of action. In these cases, sponsors were allowed to designate which Center would review their product. Not surprisingly, they chose the Center that would provide the easiest regulatory pathway. For an illustration with tissue engineered products, see L. Hogle, "Pragmatic Objectivity and the Standardization of Human Tissues," *Social Studies of Science*, forthcoming.
 10. FDA, "Performance Report to Congress for Office of Combination Products," 2006, available at <<http://www.fda.gov/oc/combination/report2006/overview.html>> (last visited August 15, 2008).
 11. Nanotechnology Task Force, Department of Health and Human Services, "Nanotechnology: A Report of the U.S. Food and Drug Administration," July 25, 2007, available at <<http://www.fda.gov/nanotechnology/taskforce/report2007.html>> (last visited December 21, 2008).
 12. The question of regulatory adequacy was also analyzed in M. Taylor, "Regulating the Products of Nanotechnology: Does the FDA Have the Tools It Needs?" Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies, October, 2006, available at <http://www.wilsoncenter.org/index.cfm?topic_id=166192&fuseaction=topics.item&news_id=202942> (last visited December 21, 2008).
 13. See Nanotechnology Task Force, *supra* note 11.
 14. Reports of political interference continue to emerge. See C. T. Whitman, Commentary "Your Inbox, Mr. President," *Nature* 457, no. 7227 (2009): 258-261 (on politicization of the EPA).
 15. R. A. Freitas, *Nanomedicine*, Vol. IIA: *Biocompatibility* (Austin, TX: Landes Bioscience, 2003): at 7.
 16. D. Williams, "Revisiting the Definition of Biocompatibility," *Medical Device Technology* 14, no. 8 (2003): 10-14.
 17. *Id.*, at 125-143.
 18. Anonymous, "Special Report: Life 2.0: Synthetic Biology," *The Economist* 380, no. 8493 (2006): 76-80; G. Samuel, M. Selgelid, and I. Kerridge, "Managing the Unimaginable: Regulatory Responses to the Challenges Posed by Synthetic Biology and Synthetic Genomics," *EMBO Reports* 19, no. 1 (2009): 7-11.
 19. See Nanotechnology Task Force, *supra* note 11.
 20. J. van Loon, *Risk and Technological Culture* (New York: Routledge, 2002): at 7.
 21. J. Kuzma and J. Besley, "Ethics of Risk Analysis and Regulatory Review: From Bio- to Nanotechnology," *Nanoethics* 2, no. 2 (2008): 149-162.
 22. J. Moreno, Keynote presentation, Launch of the Center for Nanotechnology and Society, Arizona State University, 2006.
 23. B. Gordijn, "Nanoethics: From Utopian Dreams and Apocalyptic Nightmares towards a More Balanced View," *Science and Engineering Ethics* 11, no. 4 (2005): 521-533; A. Nordman, "If and Then: A Critique of Speculative Nanoethics," *Nanoethics* 1, no. 1 (2007): 36-46.
 24. G. Gaskell, E. Einsiedel, W. Hallman, S. Hornig Priest, J. Jackson, and J. Olsthoorn, "Social Values and the Governance of Science," *Science* 310, no. 5756 (2005):1908-1909. This survey of Americans, Canadians, and Europeans suggested that while the majority of respondents felt that decisions about technology should be left to experts and based on scientific evidence, about one-third favored moral and ethical considerations over scientific evidence, and about one-quarter favored public opinion over expert opinion in decision-making. This raises questions about both public support for current science policy administration and the role of public participation in making decisions that may affect their lives and work. The authors note differences between countries as well as between types of technologies (stem cells, nanotechnology, biotechnology).
 25. Critical self-evaluations of bioethics appear in the edited volume, L. A. Eckenwiler and F. G. Cohn, eds., *The Ethics of Bioethics: Mapping the Moral Landscape* (Baltimore, MD: Johns Hopkins University Press, 2007). See also S. Jasanoff, *Designs on Nature: Science and Democracy in Europe and the United States* (Princeton, NJ: Princeton University Press, 2005): at 200, 286.
 26. A. Charo, "Passing on the Right: Conservative Bioethics Is Closer Than It Appears," *Journal of Law, Medicine & Ethics* 32, no. 4 (2004): 307-314.
 27. Susan Wolf discusses the intertwined histories of bioethics and law in S. M. Wolf, "Law and Bioethics: From Values to Violence," *Journal of Law, Medicine & Ethics* 32, no. 4 (2004): 293-306. While beyond the scope of the current paper, it is important to consider not only how law responds to technologies, but also how technologies affect law. An example of this is California's Proposition 71 and the resulting forms of state governance established to address stem cell research.
 28. See Gordijn, *supra* note 23.
 29. In fact, this is what many argue will happen with stem cell science. Drug discovery, tools for diagnostics, and knowledge of disease models may turn out to be the most important outcomes, rather than development of therapeutics.
 30. The BioBricks Foundation links not-for-profit and commercial research using an open source-style access to biological parts and information. See <<http://bbf.openwetware.org/>> (last visited August 18, 2009).
 31. Currently, viral vectors are used to ferry genes to a location for gene therapy and to create induced pluripotent stem cells, potentially inducing cancers. As much as 50% of time in surgery is spent controlling bleeding. Self-assembly gels can seal the wound and quickly stop bleeding (see Jain, *supra* note 6, at 191). Nanoneedles can be used in combination with atomic force microscopy to do "surgery" on living cells, entering the membrane while causing minimal damage (*id.*, at 60).
 32. Professional associations, codes of ethics, and agreements on definitions and classifications that occur at consensus conferences and in other venues all serve regulatory purposes as much as federal regulatory agency action does. Recommendations for more formal governance and assessment methods can be found in D. Guston and D. Sarewitz, "Real-Time Technology Assessment," *Technology in Society* 24, no. 1-2 (2002): 93-109; G. E. Marchant, D. J. Sylvester, and K. W. Abbott, "Risk Management Principles for Nanotechnology," *Nanoethics* 2, no. 1 (2008): 43-60; and J. Kuzma, "Moving Forward Responsibly: Oversight for the Nanotechnology-Biology Interface," *Journal of Nanoparticle Research* 9, no. 1 (2007): 165-182.
 33. C. Rosenberg, *Our Present Complaint: American Medicine, Then and Now* (Baltimore, MD: Johns Hopkins University Press, 2007).