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RISK AS CONTINUUM
A Redefinition of Risk for Governing the Post-Genome World

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Executive Summary

The scientific achievements of the past 30 years in molecular biology have produced an unprecedented volume of genetic material, information and experimental activity. The post-genome age began to gestate with the creation of recombinant DNA technology in 1972, which for the first time allowed genes from one organism to be inserted into another, and “officially” arrived in February 2001 with the completion of the historic sequencing of the human genome.

During that 30-year period, the products of genomic biology writ large have gradually become an integral part of the Zeitgeist — genes themselves and their various components, genetically modified and engineered organisms in drugs and food, databases filled with the genetic identities of millions of people, ever-cheaper and more powerful technology to deconstruct and analyze these tiny, potent strands of identity. Not only do these stand to permanently alter our notions of human autonomy, the natural environment and health but, perhaps most fundamentally, they force us to reconsider our definition and perception of public risk.

Protecting the public from undue risk is the job of governance. The degree to which the scientific risks posed by the products of genomic biology are still largely unknown — and the social and cultural risks mostly unacknowledged — has magnified many of the shortcomings of present-day government oversight, laws and regulations in areas where science and technology meet public interest. At the heart of these shortcomings is the fact that the post-genome world lacks a transparent framework for risk and its regulation that includes the input of all knowledgeable stakeholders affected by these decisions, while simultaneously encouraging responsible technological and economic development.

The following interdisciplinary exploration begins with an argument for redefining risk for the post-genome world. Some of the potential scientific risks are being considered for the first time in history, such as the exposure of humans and the environment to genetic pollution from modified living organisms, and engineering of the human germline cells which pass along our heredity traits to future generations. Some of the social and economic risks may have equally far-reaching consequences: the theft of genetic resources, ongoing controversies over the patenting of genes and other living materials, the privacy and civil liberties risks of compiling DNA databanks, the economic risks of commodifying living organisms.

We continue with a discussion of the benefits and drawbacks to our reliance on the data and agendas of scientists, and an exploration of the risks posed by the ongoing oversimplification of this debate. We then present a series of perspectives from various disciplines on possible ways to mitigate these risks, closing with a discussion of some new and potentially useful approaches and methods for opening the process of governance to include the full complement of stakeholders who are affected by these historic and critical decisions made on their behalf.

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[0.0] Introduction

This first issue of the Hybrid Vigor Journal has taken on an ambitious task: to begin an interdisciplinary, inclusive dialog about risk and governance in a post-genome world. Despite the enormity of the task, the topic is clearly representative of the global Zeitgeist; the questions it raises are as formidable and vital as the discussions of terrorism and war that, since September 11th, have competed for world attention with the escalating debates about genetically modified organisms, stem cell research and human cloning.

What exactly do we mean by “a post-genome world”? The genesis of the post-genome world was the creation of recombinant DNA technology in 1972, which for the first time allowed genetic material from one organism to be inserted into the genome of another, often from a different species. Thirty years later, rapid advancements in technology have allowed the sequencing — that is, the decoding of the sequence of all the DNA in a cell — of the genomes of a number of organisms, culminating in the historic completion of the human genome sequence in February 2001. The sequencing of the human genome represents a milestone — an arbitrary one, to some, but a significant one nonetheless. It marks the beginning of the post-genome era, where we now must learn to deal thoughtfully with the consequences of these transformative achievements.

These achievements in genomic biology and technology have unleashed between them a torrent of genetic material, information and experimentation, which together stand to fundamentally alter our notions of human autonomy, the natural environment and public health, and — perhaps most fundamental to all these notions — our definition and perception of public risk.

Although to focus solely on a redefinition of risk in the post-genome world would certainly be enlightening, it would be insufficient. Protecting the public from undue risk is the job of governance, and these fundamentally new notions have magnified many shortcomings of the existing patchwork of government oversight. Some of the aforementioned genetic torrent is held in check by regulation or law, some is not; some of these materials and data are monitored, some are not. Legal precedent about ownership of genetic material and information is not established or, where established, is hotly contested. Crucial decisions about what can be done with genetic materials and information, and what kinds of activities researchers are allowed to engage in, are being made by scientists, governments and industry without informed and equally weighted input from all potential stakeholders. Indeed, some of these stakeholders are not yet born or even imagined, which makes questions about genomic science even more profound than the already pernicious governance issues regarding, for example, how best to store nuclear waste.

Not incidentally, the very science upon which all this scholarly, regulatory and economic activity is based is in such a nascent stage that it seems to change almost daily. Despite what we may read or hear — or want to believe — of the promises of biotechnology and pharmacology and agribusiness, that we are teetering on the very precipice of being able to cure all diseases, feed the world, heal the planet and so on, and despite the rapid advancements that scientists and engineers have made in these areas, most responsible researchers and industry executives admit they still know very little about how genes actually work and interact *in vivo*, in the real world.

As a result, the revelation of each new discovery, often rocket-launched simultaneously into the pages of scientific journals and the popular press, is met with protests of equal velocity by those demanding that this work be halted until more is known about its long-term effects. This polarization of the debate is not useful. Given the complex and conflicting realities of human life and culture, including those by which research is funded, public perception is influenced, economies created and laws made, such black-and-white thinking works at cross-purposes.

The more fundamental issue, which exists below the level of polarized debates, is that the post-genome world lacks a consistent — and sufficiently transparent — framework for risk assessment (and subsequent governance) that both encourages appropriate, ongoing technological development while simultaneously and effectively addressing and protecting broader public interests. In the absence of such a framework, these issues have attracted the attention and concerns thousands of executives, thought and religious leaders, artists, activists and scholars from the natural and social sciences, public policy, regulatory agencies, national and international security, ethics and law. Many of them have begun to research, discuss and act upon these unfolding realities, each from his or her own bounded perspective or discipline.

What is now required is to bring those perspectives into the larger, more integrated context of risk in the post-genome world — what defines it, how it is assessed, how we might best manage and govern it — with the goal of providing a new framework in which their concerns and activities can become more purposeful. The first task of any effort that requires crossing the boundaries of expertise is to level the playing field of knowledge, to present all stakeholders — across disciplinary, economic and ideological boundaries — with clear-eyed information on the relevant issues, with full disclosure of the all the various relationships, tensions and complexities involved. These issues include not only the science of genomics, in terms of its promise, risks and present-day realities, but also the legal and economic risks, as well as some of the risks to individuals and global culture, that have stimulated today's intense debates. We realize many of these issues are still in the realm of the unknown. If we already knew and understood these issues and all their contingencies, then risk itself — the uncertainty of demonstrable harm, broadly defined — would be less the question than the task of assessing what we value and how much we value it. But it is the magnitude of what we do not know that makes the task so difficult, and so critical to begin articulating it.

[0.1] A new breed of journal

This journal is a first step toward that goal. To take on a subject of this complexity and intensity is obviously an enormous and controversial task, and given the sheer volume of information and various perspectives, this journal should not be considered definitive in any way. Its style is also likely to be unfamiliar to academics, in particular, who are accustomed to receiving their information in the proscribed formats that are specific to journals of their disciplines. As one might expect from an organization named Hybrid Vigor, these journals will be written in a way to maximize their ability to reach the widest number of readers from all disciplines — given that, as one of our advisors says, everyone is a layperson when they move outside their area of expertise.

Although we will do our best to provide a window to as much information as possible so that interested readers can take matters into their own hands, the goal of this monograph is simply to present and crystallize the issues that form and inform the Zeitgeist of post-genomic reality.

We then hope to catalyze a substantive, respectful, depolarized discussion between stakeholders in order to set the stage for effective action.

We will do so first by briefly presenting a case for the redefinition of risk, citing research and presenting various perspectives which suggest reasons for expanding today's definition beyond the walls of the laboratory where it most often is lodged today. We then will discuss the limitations of today's largely reductionist perspectives and suggest various alternatives, drawing on what we consider to be particularly relevant literature and analyses from a variety of disciplines and institutional perspectives. And finally, we will close with some suggestions from those with ideas of how to proceed.

Although it is clear there are no easy answers to any of these questions, the one position we are willing to take is this: Reductionism in any form can be dangerous. Actively acknowledging the complexities of the situation at hand by including the broadest relevant constituency in the discussion of risk is imperative in order to create a tenable outcome for the research community, industry and the public. We all deserve not simply to co-exist, but to thrive in the post-genome world.

[0.2] The researchers whose work informed this journal

This journal represents the first step in the Hybrid Vigor Institute's systematic method for solving complex problems by cultivating interdisciplinary conversations and collaborations. By means of this publication, we intend to introduce scholars who are working on similar problems, often in disciplinary isolation, to each other's work, and to foster awareness of this work within the various relevant communities.

The work and/or thoughts of the following scholars served as the foundation for this interdisciplinary examination of risk and governance. Although a much greater body of work informed this journal, theirs was the seminal knowledge (in the form of books, papers and/or correspondence) upon which the following argument was based. Any wrongful interpretations are solely the author's.

- **Kjell Andersson, Ph.D.**, principal, Karinta Konsult; Stockholm. "Transparency and Public Participation: The Need for a New Paradigm."
- **Ulrich Beck, Ph.D.**; professor of sociology, University of Munich. *Risk Society: Towards a New Modernity*.
- **Philip Boreano, Ph.D.**, professor, Department of Technical Communications, University of Washington. "Sound Science and the Precautionary Principle."
- **Roger Brent, Ph.D.**, director and chair, the Molecular Sciences Institute, Berkeley, CA. "Genomic Biology."
- **Robert Carlson, Ph.D.**, former research fellow, the Molecular Sciences Institute, Berkeley, CA; research fellow, Applied Minds, Glendale, CA. "Open-Source Biology and Its Impact on Industry."
- **Chris Elliott, Ph.D.**, Pitchill Consulting LTD; systems engineer and barrister based in the United Kingdom. "Scientific Uncertainty, Technological Risk and Public Policy."
- **Michael Fortun, Ph.D.**, professor, Science & Technology Studies, Rensselaer Polytechnic Institute. "Excess, Ethnography, Becoming-Bioethicist."
- **David Guston, Ph.D.**, assistant professor, Public Policy, Department of Public Policy, Rutgers University. "New Research on Boundary Organizations: Environmental Policy and Science"

- **Stephen Hilgartner, Ph.D.**, associate professor, Department of Science & Technology Studies, Cornell University. “Acceptable Intellectual Property: The New Politics of IP.”
- **Benjamin Kuipers, Ph.D.**, professor, Department of Computer Sciences, the University of Texas at Austin.
- **Kathleen McAfee, Ph.D.**, assistant professor, Social Ecology and Community Development, Department of Forestry, Yale University. “Economic and Genetic Reductionism in Biotechnology Battles.”
- **Peter Szolovits, Ph.D.**, professor, Computer Science and Engineering in the MIT Department of Electrical Engineering and Computer Science; head, Clinical Decision-Making Group, MIT Laboratory for Computer Science.

The next step in the Hybrid Vigor process is to use this publication as the basis for convening a working symposium of policy makers, industry representatives, natural and social scientists and other stakeholders, with the goal of creating an actionable agenda for addressing these critical problems. And finally, following the symposium, we will create a virtual collaboration zone on the Hybridvigor.net website where work on this agenda can continue toward a stated goal.

[1.0] The redefinition of risk, and our relationship to it

Why redefine risk now? Because it has been a long time since we have, and the rapid acceleration of change over the past century seems to demand it. To put it rather simplistically, in the 19th century, for example, and still today in underdeveloped countries, the risks of an industrializing society were more obvious: poverty, hunger, crowding.¹ Benefits aside (and of course there were many), risks in those days were *visible* costs. People could see them with their own eyes, feel them in their stomachs. They bumped shoulders with them on the streets.

These conditions have now changed. In today's modern society, with globalization, the onset of the information age and the ascendancy of the apparently inexorable forces of technology and science, we are dealing with the opposite: the invisible risks and threats of *possibility*. These risks have been growing for many decades in our culture, including those associated with the growth of highly industrialized agriculture and its use of pesticides, and perhaps the disposal of nuclear waste. Most relevant to this discussion were the new possibilities of risk posed first by recombinant DNA, and more recently by the sequencing of the human genome and the resultant technological developments in food, reproductive technologies, and the environment.

Some of these new, post-genomic risk possibilities include:

- **Theft**, also known as biopiracy: the economic and social risks presented by the unauthorized patenting of genetic resources taken from developing countries, and/or unauthorized access to a genetic resource and using that resource in a manner that contravenes a national regime, if one exists. A broader and more controversial definition, used by many indigenous people, includes both loss of control over natural resources, including cataloguing the native use of medicinal plants, as well as the very act of patenting life forms, in a way that is either illegal or does not fairly compensate whoever owns or controls these resources.
- **Biosafety**, which in the post-genome context is concerned primarily with analysis, containment and recovery of genetically modified or engineered organisms, or avoiding "genetic pollution" of wild species by artificially engineered species, or genes from genetically engineered species (also known as gene flow). This includes developing protocols for keeping genetically modified organisms, and the knowledge of their production, under tight control. Biosafety also includes enforcing the already existing prohibitions on the research and development of engineered pathogens for use as biological agents; devising safe ways to generate molecular mechanisms; restricting known-dangerous ones from leaving simulations to be created physically; and employing clear protocols for addressing failures.

One might also include in this category the risks of new forms of traditional human subject/patient harm. For example, Fritz Bach, the professor of surgery at Harvard Medical School who was one of the first to warn of the viral risks of transplanting organs between species (known as xenotransplantation), has described the risk as "finite but unknown." Other types of harm might result from engineering changes in genes that affect future generations, a risk that is distinct from germline engineering, below.

- **Germline engineering**, or genetic modification of the human cells which give rise to sperm and egg. Modification of the germline permanently alters genetic heredity; whether intended to correct presumed disorders or to enhance desired characteristics, it raises the risk of eugenic applications and health risks to women and their offspring. In fact, the technological sophistication of these post-genomic technologies forces us to confront eugenic questions — in

particular, drawing the distinction between “therapy” to heal and “enhancement” to improve our given lot — in a more fundamental way than ever before.

- **Genetically modified foods**, which for the first time in history extend deliberate cross-breeding beyond closely related life forms — for example, fish genes have been placed in tomatoes, human genes in tobacco, soil bacteria in corn and potatoes, and viruses in squash and fruit — to effect specific, human goals, on a scale which does not occur in nature. (Genes move naturally between non closely-related organisms.) There are many possible risks here, the overarching ones being that scientists do not know the extent of the phenomenon of gene flow, how it occurs, or its consequences. Subsequent risks of gene flow (or other unknown factors) include the reduction or loss of diversity in the food supply; contamination of water and soil; and allergic and/or toxic health reactions.

- **Genetic privacy and discrimination, and DNA “databanking”**, whereby those who collect genetic information or genetic materials from individuals for various reasons, ranging from medical testing to law enforcement, claim ownership and control over those data and materials. Risks here include, most obviously, ceding ownership of genetic materials and information to governments and corporations rather than to individuals, leading to loss of privacy regarding individual identity, potential abuse by government and law enforcement, as well as commercial exploitation by biotechnology companies and/or discrimination by insurance companies due to the detection of genetic susceptibility to various diseases.

- **Life patents**, the means by which commercial enterprises claim proprietary legal and commercial rights to the use, manufacture or sale of genes or genetic sequences, whether plant, animal, or human. Critical questions must be answered regarding the circumstances under which anyone, other than the individual donor, can legitimately “own” or control, via patents, some or all of an individual’s genetic information, and under what circumstances. Acknowledged risks to date include a resultant increase in the cost of medicines, retardation of progress in medical science, and premature and insufficiently tested interventions in major food crops and living beings. Of equally vital concern is the legal shielding of, or requiring payment for access to, important research data and medical care. Some cultures also fear patents will cause homogeneity in food sources, making them more susceptible to catastrophic diseases, and loss of control over their natural resources.

[1.1] Front-line arbiters of risk: The natural sciences

Modern risks, of course, existed long before the genome was sequenced. The evaluation and management of these risks has become both a science and an industry unto itself. The most visible to ordinary people in their daily lives is actuarial science, whose focus is on managing the financial and economic consequences of risk and uncertainty. But while actuarial science uses sophisticated logic and mathematical models to approximate the probabilities of economic risk, the identification and analysis of risks to human health and the environment begin first in the realm of the physical universe.

Governing bodies (including, but not limited to, the Environmental Protection Agency and the Food and Drug Administration in the United States, the Departments of Agriculture, Defense and Energy, and their counterparts in other nations around the world) use scientific data derived from experiments conducted in laboratories and animal and human trials as their primary information source for establishing acceptable levels of public risk and potential harm. Thus the natural sciences — chemistry, biology, physics — are first in line as arbiters of potential risk. Although what leads to a final, scientific determination of risk is obviously a complex calculus, let us leave aside the details for the moment — they are significant, but only partially relevant to the

larger discussion — and look at the level of risk protection provided by reliance on what might be called the “expert-science” approach.

As the German sociologist Ulrich Beck writes in his influential 1992 book *Risk Society*, the risks of modern culture — in this context, particularly, those that spring from the rapid acceleration of scientific progress — differ fundamentally from the previous era because they are not visibly social or economic byproducts of industrialization. Instead, modern risks cut across social strata, are largely invisible, and generally only become part of our consciousness when we are told of them, or when their latency comes to an end and they become manifest. Not incidentally, as noted by some of the risks outlined above, where many of the risks of the industrial age were local to people and communities — the risks of burning coal, using asbestos, child labor and so on — our shrinking, “globalized” world means that the small manipulation of a gene in a laboratory may potentially have huge effects across a very broad, potentially unbounded scope of place and time.

In other words, my ability to avoid any eventual victimization I might suffer by eating tomatoes laced with fish genes cannot be driven by my own perception until (or unless) the risk becomes reality; such a determination is outside the reach of my experiential knowledge. If I want to protect myself, I have no choice but to depend on what I am told. Thus the quality of external knowledge, and my access to it, and its accuracy, trustworthiness and credibility, are key to my ability to realistically assess this new class of risk. As Beck writes, not particularly generously, “We no longer pick the experts — instead, the experts choose their victims,” based on the information they provide.²

Here, then, as ridiculous as this idea might seem to a scientist, whether the risks themselves do exist becomes less critical than the fact that they *might*: how the risks themselves are decided to be risks, and by whom. As said above, since the data upon which these decisions rest are first decided by (natural) science writ large, and only later enacted by various governing bodies and/or deployed in commercial products, the validity and credibility and transparency of the scientific endeavor itself takes on dramatically increased importance.

[1.2] The paradox of risk and expertise: Science is fallible

So herein lies the paradox of risk determination today: Obviously, much of the planet’s health and well being is at stake if the “experts” in whom these decisions reside are wrong — even though *it is a completely expected and normal state of affairs for scientists to be wrong*, to test and critique each other’s results, and iterate new approaches and conclusions as they progressively glean knowledge from their mistakes. Laboratory science is, by both definition and practice, consistently and predictably fallible.³

Thus the fact that governing bodies rely on a scientific community that operates in relative isolation, with a de facto precarious claim to authority over “acceptable risk” decisions, is not only unfair to the public (and the planet). It also presents what should be perceived as an untenable situation for researchers who make such determinations in these new, risky arenas, by asking them to bear the brunt of responsibility for regulations, decisions and side effects over which they have only a narrow range of control.

In truth, many (if not most) scientists will not see the picture this way. Although they may know and even embrace their fallibility amongst themselves, many of them have grown accustomed

to the moral authority they've been granted in modern society, even if it makes them responsible to an unfair and possibly dangerous degree for many of the risks of modern life. In order to more fairly and effectively distribute this responsibility, a new definition of risk must both embrace and extend beyond reproducible results and the calculations required of scientists — regarding “acceptable levels” of toxicity, deaths per million, deformities and the like — into a broader assessment of risk based on what Beck calls cognitive sociology: “not only the sociology of science, but in fact the sociology of all the ... agents of knowledge in their combination and opposition, their foundations, their claims, their mistakes, their irrationalities, their truth and the impossibility of their knowing the knowledge they lay claim to.”⁴

Since in the modern world risks originate in knowledge and norms, the *perception* of risk and the *risk itself* are not different things but one and the same. Thus a more effective definition of risk would address both with the same attention and care. This is not to say that such a method can easily be derived or practiced. Consensus may not be possible. Obviously, outliers on the curve in either direction — from pure bio-Luddism to techno-fetishism — will not have their way, and deciding who gets lopped off as too extreme will be difficult for all involved. But the potential that the process may be fraught is insufficient grounds for not expanding the risk debate.

The potential consequences of not redefining and redistributing the consequences of risk go far beyond the limited ability of science to address our fears of unintended consequences, or side effects, to living beings and the ecosystem. As Beck notes, there could be dire “social, economic and political side effects of these side effects,”⁵ including all the risks noted above, as well as market collapses, new political and legislative pressures, global activism that halts technological progress, recognition of compensation claims and other great economic costs, legal proceedings and more.

Ironically, of course, these are the very types of consequences which government and industry are hoping to avoid by trying to maintain the status quo. But the status quo — where specialized experts inform policy makers, and that is often the extent of the debate before laws and regulations are enacted — has so far proven woefully inadequate for addressing the growing concerns of a global population about the risks of a post-genome world. To address these concerns demands a more inclusive approach, for two very important and related reasons: One, people have access to more and more information (whether it is accurate or not, an issue we cannot adequately address here); and two, to maintain the status quo without directly addressing their increasingly informed concerns is undemocratic, or at the very least asking for trouble on a global scale. Again, according to Beck:

Risks ... fall through the sieve of overspecialization. [Risks] are what lie *between* the specializations. Coping with risks compels a general view, a cooperation over and above all the carefully established and cultivated borders. Risks lie *across* the distinction between theory and practice, *across* the borders of specialties and disciplines, *across* specialized competences and institutional responsibilities, *across* the distinction between value and fact (and thus between ethics and science), and *across* the realms of politics, the public sphere, science and the economy, which are seemingly divided by institutions.⁶

If we accept this definition of risk, then the engineers and scientists who work in the realm of genomic biology may have a decision to make: they can continue to cooperate with the present system of governance which determines risk by narrow, physical definitions, and continue to be the single focal point upon which an increasing number of critical, life-altering decisions rest. Or

they may choose to expand their definition by welcoming the opportunity to share responsibilities with knowledgeable others, and develop a new, inclusive process of exploring, defining and managing risks in the service of public safety that embraces ongoing iterations and changes in science, rather than trying to avoid or undo harm done.

Call this expanded definition, perhaps, “risk as continuum.”

[1.3] Challenging their own status quo

Scientists who take on this task will find themselves challenging their own fundamental ideas of rationality, knowledge and practice, as well as the institutional structures in which these are put to work. Of course, to accept these challenges will fundamentally change the relationship between governance and science and the current process of risk evaluation, introducing new risk/possibilities previously unencountered and unacknowledged, as well as ambiguities, complexities, and the dreaded “irreproducible results” of social science and analysis. A larger debate, one where science with a capital “S” is not expected to produce truth with a capital “T”, which is then acted on by regulatory and legislative bodies who are under constant political pressure, would produce a new and far more constructive paradigm for the governance of risk.

But scientists and engineers should not be asked to accomplish such a massive shift alone. The knowledge they produce, and the risk decisions they are asked to make based on that knowledge, are both greatly influenced and ultimately implemented by governments, academic institutions and industries around the world. In order to make informed determinations together, these groups will also need to critique their processes and procedures, and open them to outside examination, to a far greater degree than they have been willing to do before now. This is likely to be particularly true of biotechnology, pharmaceutical and agricultural biotechnology companies, where the tension between profit motive and public interest has spawned the most visible discord in the post-genome world to date. (Of course, this is not unique to the post-genome era; it simply has farther-reaching potential consequences.) The process which funds university research is likely come under greater scrutiny as well.

This is not to say that the process of inclusiveness is itself without risk. There is also a risk that such self-examination by all parties may cause scientific and technological progress as we know it today to suffer death by a thousand cuts, with some of the great potential benefits of genomic biology never making it past the navel-gazing phase. But this outcome will not generally be in anyone’s best interest, and in any case, many far more unpleasant paths than self-examination could yield the identical result. Given the growing unease with which many global stakeholders view “progress” in the post-genome world, and its many negative potential consequences as outlined above (and below), there appears to be no choice but to at least consider new ways to address these issues if we are to create a regime that will minimize the inevitable negative and unintended consequences for the environment, health and human freedom.

[2.0] Genes are/not Legos: risks of genetic reductionism, writ large

At the heart of the risk discussion in the post-genome world is genetic reductionism. In fact, the issue of reductionism in several forms — genetic, economic and legal — is as basic to our argument as the redefinition of risk itself.

Before we begin to detail that argument, it is important to note a critical semantic distinction regarding the term “reductionism.” Virtually all scientific endeavors throughout history would have been impossible without reductionism. The ability to reduce a problem to its components in order to conduct experiments and derive useful data is the only way to begin to make sense of the natural world. The process of science employs a certain kind of simplification that is critical, and for that, its central dogma — that, say, experimental results are 80 percent correct more than 80 percent of the time — has been vital.

On first examination, this dogma seems to be particularly true of the study of genes. In 1857, Gregor Mendel discovered that there was a single entity — a gene — that controlled whether pea plants had green or yellow seeds and pods, or grew tall or short. The field of genetics which Mendel pioneered is based on the presupposition that genes can, in fact, be successfully treated as indivisible units of heredity. And to a significant degree, that has proven to be true.

Although the scientific life of a molecular biologist is about successfully treating genes as discrete units, the responsible ones will also readily assert that finding a “gene” that may be responsible for baldness, for example, does not mean that they know enough about the complex systems surrounding genes and gene expression to declare an imminent cure for the condition simply by replacing the poor performer.

Based on most of the public knowledge about genomics, however, this truth is not readily apparent to the lay public, and leads to our second definition of reductionism, more relevant to this discussion.

An increasing number of researchers who study the post-genome Zeitgeist are concluding that today’s reductionist *presentation* and *discussion* of the scientific risks and economic and cultural considerations presented by genomic research and developments does more than simply downplay the enormous complexity of the scientific endeavor. Instead, such oversimplification dangerously obscures the truth — dangerous particularly because these reductionist perspectives are what largely inform industrial and public policy in this realm today, no matter how truthfully and in what context scientists actually report their results.

In this context, a definition of genetic reductionism, or “molecular-genetic reductionism,” as Yale University professor Kathleen McAfee states it, would be the conceptualizing of genes as “unitary, moveable objects, with stable, predictive properties.”⁷

In other words, genetic reductionism treats DNA as though it were composed of Lego parts: it posits that functionality can be snapped in and out of the sequence like so many arches and bricks; technicians can replace a damaged gene with a whole one, or a poor performer with a robust one in any given organism.

The promised benefits of a biology which consistently behaves this way are truly magnificent, and for the past several decades, solely on the strength of such promised magnificence, have

yielded (and lost) billions of dollars in speculative research and development funds for universities and biotechnology investors, and spawned entire new industries. Any Day Now we are to expect genetic engineering to produce vastly increased crop yields and the ability to grow food in formerly hostile climates; to engineer foodstuffs that contain or manufacture vaccines; to render disease-bearing organisms impotent; to allow drugs to be tailored to an individual's genetic profile.

These promises are supposed to come to fruition by exploiting new techniques for mapping and manipulating genetic material that allow genetic engineers to know exactly which Lego-gene they are moving from one organism into another, precisely how that bit of DNA will act in the new organism, and exactly what expressed trait or behavior will result from the transfer.

But if this oversimplified conception of genes were true, there would already be many more success stories to date for genetically modified organisms and the products containing them. A few examples to prove the point: Some studies on "Bt" potatoes, corn and cotton — modified with genes from the *Bacillus thuringiensis* (Bt) soil organism that acts as a pesticide to certain insects when ingested, supposedly obviating the need for chemical pesticides — have shown that third and fourth generation pests who feed on it can now withstand higher doses of the pesticide than before; and also that Bt crops and their pollen can sicken or kill some "non-target," or beneficial, insects, including Monarch butterflies.⁸

Although there have been both successes and failures, genetically modified crops have overall not produced higher yields, nor have they been less costly for farmers. In fact, according to data from the Organization for Economic Co-operation and Development (OECD), 73 percent of the genetic modification in agribusiness products is designed not to "naturally" repel pests without the application of additional chemicals, or improve crop yields or nutritional value, which was the original "feed the earth" promise. Instead, they have been designed solely to withstand the application of herbicides, keeping the existing market strong for agribusiness concerns who produce and sell both seeds and herbicides.⁹

The success rate of forays into genetically modifying animal organisms (including humans) is hardly more encouraging. Most of the cells or embryos into which technicians attempt to insert new genetic material die, or are deformed, or fail to take up the new genetic construct, or "carry" (accept) the gene but fail to express the desired trait. It typically takes hundreds or even thousands of failed insertion attempts to produce an organism that displays the desired trait, or a cloned animal that survives without debilitating deformities. The scientists who conduct this research know that we are many, many years away from being able to consistently replicate positive results.¹⁰

[2.1] Fruits of genomics: yet unripe

This is emphatically *not* to say that genetic engineering holds no promise, or even that it has been a failure to date. The point is simply that the public portrayal of genomic biology today is a dangerously oversimplified, premature representation of that promise. As stated earlier, particularly in the developmental stages of a nascent realm of knowledge, a high ratio of failure to success is the nature of the scientific endeavor, thus entirely predictable to scientists working in the field. Their experience in the lab only highlights what academics such as McAfee, who literally toil in the fields, have known for years: that life in its full complexity is still deeply

mysterious to science, understood not at all to the level that public pronouncements and promises would have us believe.

Today's widely touted, simplistic view of genetic engineering plays well in the press, but ignores the fact that most responsible scientists repeatedly assert that they know a tiny fraction of the mechanical dynamics and interactions that take place between genes, molecules and other cells; how cells work within the physiological systems of living bodies as well as outside of them, in agriculture and the larger ecosystem; between complexes of organisms and their geophysical environments; and the interactions between natural environments and their social co-determinants."¹¹

McAfee's condemnation of genetic reductionism as an environmental researcher — she is on the Department of Forestry faculty at Yale — is echoed by medical researchers as well. "It would be revolutionary if we could determine the genotypes of the majority of people who will get common diseases," wrote Neil Holtzman of Johns Hopkins Medical Institutions and Theresa Marteau of Guy's King's and St. Thomas' Medical School, in the *New England Journal of Medicine*. But "the complexity of the genetics of common diseases casts doubt on whether accurate prediction will ever be possible."¹²

"Ever" is almost always too strong a word to use in connection with medical science; in this case, rapid progress is being made with the development of technologies to analyze the SNPs (single nucleotide polymorphisms, the common DNA sequence variations among individuals) that provide markers to certain diseases and allow researchers to home in on disease-related mutations. Nonetheless, researchers note that there are still many variables — including the aforementioned genetic complexity of diseases, and the relative ease with which samples are contaminated — that need to be addressed before these technologies can be considered truly predictive.¹³

A research report titled *The Fruits of Genomics* jointly published in January 2001 by the consulting firms Lehman Brothers and McKinsey raised other, troubling questions for the drug breakthroughs promised by sequencing the genome. The report stated its surprising discovery that genomics "threatens to increase not only the associated research and development costs, but also the average cost per new drug"¹⁴ as researchers in search of a target are forced to sift through the staggering amounts of data produced by sequencing the genome. For example, while gene sequencing has become industrialized, "target validation" — the causal linkage of a biological function to a defined target for a drug-screening or drug-design program — is still a craft, and not many people have the requisite skills for this fundamental task.

In addition, the discovery of new genes moves researchers into new, uncharted territories of chemistry. Drug ideas may survive the first phase of testing, then run aground at the expensive, second phase, when effects on human chemistry are tested. Overall, compared to today's already astronomical costs for standard methods of drug discovery and development, the report concludes that genomics-based drugs will take longer to research, produce more non-starters, and be more costly to bring to market. This despite the fact that another of the often-repeated promises of genetic medicine is greatly reduced drug development costs. As scientists gradually learn the mechanics of interactions between genes, cells and larger biological systems, this will no doubt happen. But these discoveries are not imminent.¹⁵

Parenthetically, although one could say that the cost is a separate issue from reductionism, it is highly relevant in the context of social risk. How much a company or the government will invest to cure cancer, for example (which so far is billions of dollars to no avail), may be less the issue than how much it will cost individuals to pay for the treatments once they are developed.

Molecular biologists with great faith in the promise of genomic science are less skeptical about eventual outcomes, but nonetheless express realism to each other regarding the near-term utility of genomic data. According to 2000 article in *Cell*, the journal of record for the field, contemporary molecular biologists justifiably harbor “a degree of cynicism about the genomic enterprise” for three reasons.

First, the article states, genomic data themselves do not add enough value to help answer questions about the mechanics of how cells operate; i.e., how they make decisions and regulate themselves. Second, the data themselves are prone to errors; some sequence data are “outright falsehoods” at the moment they are annotated. Once someone enters into a database that a certain sequence, for example, is 90 percent identical to a turkey feather protein and may be involved in pigmentation, that piece of data — which could easily be totally false — is the basis for similar decisions by anyone else who uses the database, creating a cascading error effect not dissimilar to the old game of “telephone”.

And finally, with the exception of sequence data, the methods and logic used to make inferences from genomic data are “crudely observational” — that is, biologists are only able to use it to observe obvious changes that can be detected without any thoughtful, analytical understanding. Like the 1’s and 0’s which ultimately comprise computer languages, there is too much of it, and it is not sufficiently abstract to help biologists design more sophisticated experiments and derive useful biological statements. “For these reasons, information gained from genomic data rarely rises to the level of the conclusions that biologists prefer but often hovers at the level of suggestion, indication, inference, or testable hypothesis.”¹⁶

Even Craig Venter, the former president and chief scientific officer of Celera Genomics, the company which made history by mapping the human genome in tandem with the National Human Genome Research Institute, issued a strong (and quintessentially Venteresque) warning against reductionism almost immediately after the job was done: “With this technology, we are literally coming out of the dark ages of biology. As a civilization, we know far less than one per cent of what will be known about biology, human physiology, and medicine. My view of biology is ‘We don’t know shit.’”¹⁷

It is difficult to square these statements with the promises of imminent genetic utopia by biotechnology and pharmaceutical companies; at the very least, they are a convincing argument that reductionism has too greatly influenced how the larger world regards the near-term promise of genomic biology. It is clear that the science is light years ahead of where it was 10 years ago, and much of incredible value has been learned. But one percent is still one percent.

[3.0] The post-genomic risks of economic and legal reductionism

Economic reductionism in the post-genome world feeds off genetic reductionism, and by introducing the powerful motive of profit, stands to greatly magnify its risks. As McAfee describes it, economic reductionism “constructs genetic and other natural resources as quantifiable commodities,” separable from the natural environment in which they exist, thus are subject to market exchange as “intellectual property” that can be owned and sold.¹⁸

Economic reductionism is the basis for political-economic efforts such as gene patents and DNA databases, protection for which have already been widely granted, as well as the World Trade Organization’s controversial TRIPS (Trade-Related Intellectual Property Rights) agreement (more on this below), which set the global policies by which companies can trade living, modified organisms across national boundaries.

Patents on life forms in general have provoked fear and no small degree of loathing in the scientific community. Since 1980, the U.S. Patent and Trademark Office claims to have granted more than 20,000 patents on genes or other gene-related molecules for humans and other organisms. In August 2001, the office said it had more than 25,000 applications outstanding that actually claim genes or related molecules.¹⁹ Other sources claim the number of patent applications for genes and various molecular compounds over the past five years alone is more than 90,000, which is probably more realistic given that many patent applications contain multiple genes.

Patents do not confer ownership to the patent holder. Instead, in the United States at least, a patent grants a 20-year monopoly which prevents others from making, using or selling a particular sequence in a specific application without express permission from the patent holder. However, this is a distinction which many find merely semantic. Scientists in particular are deeply concerned that the commodification of critical, basic scientific discoveries will limit affordable (or any) access to genetic information, thus sharply curtailing their ability to openly conduct and publish research in a highly complex, interdisciplinary and nascent field of study.

[3.1] A gene patent is a real monopoly

As one researcher from the Human Genome Project noted, “If you have a patent on a mousetrap, rivals can still make a better mousetrap. This isn’t true in the case of genomics. If someone patents a gene, they have a real monopoly.”²⁰ An often cited example is that of Myriad Genetics Laboratories Inc. of Salt Lake City, which holds U.S. patents for sequences of the breast cancer gene BRCA1. Myriad gained swift notoriety in the research and medical community for its actions against the University of Pennsylvania’s Genetics Diagnostics Laboratory, which claims it was refused permission to perform BRAC1 diagnostic tests for members of a National Cancer Institute-funded research network. At the time, Myriad’s president said before he would grant licenses for various functions, “We have to ask, what is the research question?”²¹ Many scientists were scandalized — not only by the audacity of the question, but that the person asking it had the power to actually demand the answer and control the conduct of their research.

The argument for life-form patenting is, obviously, an economic one: industry proponents say such patents encourage investment in genetic research by both private corporations and today’s heavily corporatized universities which have become enthusiastic participants in the patent process. Although some say that gene patent ownership is so important to the portfolios of

companies that to threaten their viability would cause a market upheaval, opponents argue that the cost of identifying the function of a gene is a fraction of the cost of turning that gene into something useful, such as a drug. They say that the biotech industry in general, and pharmaceutical companies in particular, might better serve their own researchers and more efficiently spend shareholders' money if they focused on patenting drugs instead of genes, and let the researchers of the world work freely with what nature hath wrought, in the same way they do with the body's chemistry today.

Some researchers and biotechnology companies say that patenting genes, or methods for performing critical functions on genes, is a defensive move against giant pharmaceutical companies which would prefer that the only patentable commodities are the molecules they create using genetic materials and methods — the rest, they say, is “basic science”. This sharply decreases the economic viability of biotech companies and universities by redistributing all the wealth in the industry to the big players, so the argument goes, because they cannot collect licensing fees. But this speaks only to the fact that the present system for rewarding the creation of intellectual property is not only inequitable, but wrongly based on a system that rewards innovation rather than equitably distributing economic gain. [A detailed discussion of this issue is below.]

In addition, treating the genetic components of organisms as ordinary, tradable commodities, subject to private property claims and standardized rules of transnational commerce, has generated much discord in the international community, which has become highly sensitized to possible colonization by genetic technology superpowers such as the United States. Environmental economics are much more complex than trading cars or soap. These economics impact food supplies and human health, and include in their purview critical issues regarding the rights of nations to set their own priorities and make their own impact assessments. They also provide a stark illustration for Beck's notion that the possibility or perception of risk is as significant as the risk itself. According to one African ambassador, speaking at the World Trade Organization meeting in Seattle in 2001, the WTO's TRIPS agreement will “create the potential for disastrous conflicts between the technologically advanced and the less technologically advanced countries. It will endanger the traditional rights of farmers and of local communities all over the world.”²²

Another risk is that the patenting and commodification of genetic resources will encourage what amounts to strip-mining the world of its genetic resources, a process which is already well underway and, by some accounts, is already a done deal. The Diversa Corporation, for example, which lists 45 patents on its website, uses its proprietary DNA extraction techniques to, as it says, “access genetic material from uncultured organisms that account for over 99% of the Earth's untapped biodiversity”. It then sells access to this genetic information to its partners in pharmaceutical, agricultural, chemical processing, and industrial markets.²³ Although some indigenous and activist groups believe that patenting any genetic resource that in some part pre-exists in nature amounts to theft, the narrower and more workable definition — that a corporation or institution gains unfair or illegal access to a genetic resource, modifies it into an “invention,” and files a patent application for it — is still troubling.

[3.2] Toward an ‘open source’ biology

An independent, non-profit research institute in Berkeley, Calif., would like to obviate some of the more critical risks of economic reductionism by instigating what it is calling “open source

biology,” fashioned after the “open source software” movement. Open source software, unlike its commercial counterpart, is defined by the fact that the original code (the “source”) of any open source program must be freely distributed to all users and programmers, who are equally free to modify and/or improve it as they see fit. Commercial software firms, by comparison, legally bar anyone other than its designees from altering its source code in any way without explicit permission.

The theoretical underpinning for open source, which has proven to be a great success in the software world (particularly for the global Internet, much of which runs on open source software), is that when programmers can read, redistribute and modify the source code for a piece of software, thus can see and learn from each other’s work, the very best of breed steps up to the task. And as a direct result, the software evolves, improves and adapts far more quickly and with much higher quality than commercial software.²⁴

Translating this meritocracy into the world of genomics, the Molecular Sciences Institute — co-founded by the godfather of molecular biology, Sydney Brenner, and Roger Brent, a professor of genomics for 25 years at Harvard Medical School — has begun developing the foundation for open source biology. Its intention is to create a community that will build and maintain a repository of publicly available genomic technology and components. These data, cells, protocols, algorithms, genes and genetic sequences will eventually comprise a system that is roughly analogous to a computer operating system for phage, bacterial, viral, plant, and animal systems. As with the open source software movement, MSI suspects that open source biology will attract a pool of talented researchers and engineers who will contribute time, energy, data, “parts” and expertise for both the sheer intellectual pleasure of it, and from a desire to make a meaningful contribution to *public* science.²⁵

In a letter to one funding agency on the subject, Robert Carlson and Roger Brent write, “We believe we are working towards the day when well-characterized molecular components, and the know-how to use them to design and implement new biological systems, will be available to anyone who wishes. Like the software movement from which it takes its name, the Open Source Biology community will rely on individuals and small groups of people to take charge of (and receive credit for) maintaining and improving the common technology, open to all, usable by all, modifiable by all. We believe that this development will have a number of positive consequences and that it may decrease the probability of some negative ones.”²⁶

As Brent says, “reasonable people can disagree about this,” and do, particularly in a post-911 world where we now officially live in some degree of anticipation of attack by biological agents. To date, the U.S. government’s position on biological warfare has been not to restrict the flow of information — what Brent calls “the inevitable democratization of biotechnology” — but to use our superior knowledge to stay a step ahead of bioterrorists. The genetic sequence for anthrax, for example, was posted on the Internet the month after the September 11th attacks — an effort that was paid for by the government. Where one draws the line, what kinds of information should be openly available, is a debate that needs to be fully engaged.²⁷

On the positive side — in agriculture, for example — such a publicly available repository of biological parts and data might pre-empt the budding oligopoly of agricultural biotechnology companies “and the consequent higher prices and delays to innovation that will result. ... That is, while development of proprietary [biological components] may be beneficial for a very few

individual corporations, the economy as a whole will be stunted by a lack of competition and diverse innovation.”²⁸

Taking another cue from its software counterpart, MSI believes that a community of open source biologists and engineers might develop not only more robust biological components and systems — collections of components that together catalyze some activity, such as “turning on” a gene— but would also simultaneously develop biosafety protocols that could quickly contain and fix the inevitable errors that result from experimental research, in the same way that open-source software proponents reflexively generate “bug fixes” today. The open-source model might also reduce the sensitivity of engineered systems to deliberate acts of sabotage (“viruses” in both the metaphoric and actual sense) by ensuring that the knowledge about to work around complex biological systems is widely distributed throughout a “self-confident, self-aware” community.

“To make this example specific, we think it would be a shame if, in 2009, most of the wheat in this country was dependent on [a bioengineered system] of the quality and stability of Windows95,” the notoriously awful Microsoft operating system of some years back, the authors write. “Open-source biology will aid in maintaining a technological edge through diversified research. Like other distributed systems, biological research and biological engineering efforts conducted in an open source manner will be robust and adaptive, providing for a more secure economy and country.”²⁹

[3.3] The risk of limiting access to information

The issue of ownership of the staggering amounts of genomic data being generated by various commercial enterprises only exacerbates another economic — and scientific — risk: the fact that limiting access to information will slow its analysis, limiting in turn scientists’ ability to use it to solve problems or create new products. In the field of astronomy, for example, more than 40,000 CDROMs — some 24 terabytes of data — are being generated every year.³⁰ As a result, there is a global movement underway for individual astronomers to give up individual property rights to the data they collect and deliver the information into various “virtual observatory” projects in Europe, the United Kingdom and the United States. A collection of interoperating data archives and software tools, these virtual observatories utilize the Internet to form a scientific research “environment” in which astronomical programs can be conducted. In much the same way as a real observatory consists of telescopes, each with a collection of unique astronomical instruments, the virtual observatory consists of a collection of data centers each with unique collections of astronomical data, software systems and processing capabilities.³¹

Because of the sheer size of the data sets in question, scientists believe the creation of virtual observatories is critical; otherwise great potential for discoveries will remain “unexplored and underexploited” because these large data sets are now unconnected. Joining them into a uniform and interoperating database will make feasible entire new areas of astronomical research.

It is not difficult to see the parallels in the post-genome world. Although it is very difficult to get one’s hands on the size of the data sets in question, there are billions of bits of data published just to represent the human genome sequence. This does not count all the various kinds of gene-expression data, and the proprietary data generated by companies that collect and analyze genetic samples of various types. Beyond the staggering size of the databases

themselves, even if all the data were openly available to the public, few are capable of exchanging data with each other. If the Lehmann McKinsey report cited earlier is true, hoarding of proprietary data as well as its lack of interoperability could well leave many breakthroughs undiscovered.

[4.0] Legal reductionism and intellectual property: ‘Innovation’ v. ‘rights’

The third component of the post-genome reductionist triangle is what could be called legal reductionism, or the making of laws and regulations based upon these previously stated, overly simplistic notions of both genetics and economics. Most of the laws that are raising hackles today are specifically concerned with intellectual property — that is, who should be allowed to “own” genetic material or information, and under what circumstances.³²

Gene patents are issued based on the notion of innovation in biotechnology. Naturally-occurring life forms, from plankton to people, cannot be patented. But engineered plants and animals, such as genetically modified corn, or lab mice designed to be prone to cancer, can. So can the naturally-occurring chemical codes and substances which allow all plants and animals, including humans, to function on a cellular level — like genes, or hormones — as long as the “inventor” can specify a use for them.

The filing of a patent application presumes that something beyond the information relating to the genetic resource has been developed; namely, an invention.

This perspective — that intellectual property (IP) is created in relative isolation, and concerns only the immediate parties involved — was once widely accepted. But beginning in the 1980s, and with much greater intensity in the 1990s, a variety of actors emerged in the intellectual property arena with quite a different perspective. Many non-governmental organizations, academics, scientists, industry groups and governments began to view intellectual property not as an isolated result of “innovation,” but instead as a political choice with profound stakes for society and culture. As a result, according to Stephen Hilgartner, a professor in the Department of Science and Technology Studies at Cornell University, “There is a growing sense that the intellectual and institutional foundations of IP policy are too weak to manage its newly recognized political dimensions ... Nowhere is this more true than in biotechnology, where controversies about the ownership of knowledge and biomaterials are incurring profound public anxiety.”³³ What follows in this section is a summation of Hilgartner’s recent work on the subject.

Hilgartner’s argument is that the “innovation” premise for intellectual property disregards the complexities of politics, law and ethics raised in virtually any discussion of intellectual property today. He argues that the notion of innovation should be discarded, and that legal theories of property offer a more useful alternative for framing the new political and social dimensions of IP.

Law frames property as a bundle of rights, inextricably woven into a fabric of relationships, expectations, entitlements and obligations. Even people who believe they “own” real estate actually only own a set of limited rights to use the material entities; in addition, they “own” a set of obligations to prevent dangerous conditions, and provide entitlements to non-owners for damages if they fail. Property rights connected to a house radiate outward, weaving a network of legal, ethical, economic and political relationships.

In this framework, says Hilgartner, the “rights” perspective for ownership of genetic material is a more appropriate starting point for the discussion of IP in the post-genome world. Because it is not confined solely to the rights that arise during the innovation process, a rights perspective can address a wider variety of potential risks and conflicts, and include a wider group of stakeholders. At the same time, it is flexible enough to embrace the important economic and scientific motivations provided by innovation-centric theories, such as how best to encourage

invention and discovery. Innovation-based IP laws do not provide this same openness and flexibility.

[4.1] 'Private science' and the public interest

During the 1980s, legislation in the form of the Bayh-Dole Act was passed by the U.S. Congress to encourage technology transfer to the private sector in the name of national competitiveness and economic growth. For the first time, the Federal government allowed private corporations to own or control royalty-free, taxpayer-funded research. Decried by some as the rise of "private science," the resulting commodification of knowledge led to the development of new, hybrid research networks — between university and industry, the public and private sector, and basic and applied science. As a result, and not surprisingly, it was not long before problems arose regarding corruption and conflicts of interest that restricted scientific openness. In the post-genome world, scientists objected to the expansion of IP into areas that were formerly considered public domain, such as expressed sequence tags (short strands of DNA which can be used to help identify unknown genes and to map their position in the genome) and research tools. There was a growing sense that clear boundaries were not established between ill-defined biological systems and the more "textual" nature of DNA codes, and that the public domain was being restricted for commercial gain without considering the consequences.³⁴

Conventional IP protection reflects a rather romantic notion of invention and authorship; the image of a lone inventor or author in her garret, building a better mousetrap or writing a brilliant symphony. It is focused on the need to reward and incent this solo creativity, and to prevent its premature appropriation. But genomic biology and biological research are fundamentally different from these activities. They are not isolated practices. Their work occurs in networks, often geographically distributed, composed of teams of scientists from many disciplines and organizations that can span government, academic and industry organizations in a single project. This reality begs a broader perspective.

Because they have a strong motivation to help scientists, an increasing number of patient groups, health activists, and populations whose DNA has been sampled believe they have a right to a voice in the process of the research itself, as well as in the use of the results.

Hilgartner cites the example of the Canavan disease gene, where a family afflicted by the disease initiated an effort to find the gene. They raised funds, collected DNA samples, and attracted researchers to the cause. After the gene was found, the researcher who identified it and his employer, Miami Children's Hospital, patented it and began charging royalties on a genetic test to screen for the disease. Patient groups filed suit, claiming misappropriation of trade secrets by using their children's DNA without consent to obtain a patent (more later on the notion of informed consent).³⁵

Another example, from 1990, was the case decided by the California Supreme Court in favor of the University of California at Los Angeles, which was sued by a patient named John Moore, who was treated for a rare leukemia at the UCLA Medical Center in 1976. His doctor, David Goldie, removed his spleen as part of the treatment — then went on to patent a cell line in 1984, using Moore's diseased spleen, that produced proteins valuable to the human immune system.

Moore sued, claiming the university, the researchers, and two biotech firms had misappropriated his spleen and commercially exploited it without his knowledge or consent.

(The cell line's value had been estimated at \$3 billion.) He lost, while the president of the Industrial Biotechnology Association, a trade group, called the ruling "a very big victory" for biotechnology that had biotech companies "breathing a sigh of relief."³⁶

It seems logical that potential beneficiaries of emerging genomic technologies, also known as "consumers" in this context, should have a right to share in the "property" that they participated in discovering. Through the lens of the "innovation" perspective, however, this logic is entirely absent.

[4.2] Frontier, or the 'New Colonialism'?

Many people envision genomic biology as a new frontier, where isolation of genetic sequences constitutes true novelty, a move into unexplored territory that by definition cannot impinge on earlier rights. But a look back at the history of colonialism shows that land perceived as uninhabited is sometimes already occupied by others. Again, through the lens of innovation, gene-based IP is an unpopulated landscape. But from the rights perspective, clearly it is not.

A useful example comes from plant engineering. When a company inserts a gene into an existing plant variety and patents the result, the innovation may add value, thus from the innovation perspective the patent is just. But the rights perspective would point out that the patent appropriates not only the value of the new gene, but also the value of the original variety (an observation which provides yet another argument against genetic reductionism as well), and expropriates the value of the gene as it pre-existed in nature.

An example of the limitations of this perspective is so-called Terminator technology, sold by a subsidiary of Monsanto called Delta and Pine Land Co., which genetically alters the seeds of certain food crops to only survive for a single generation, thus preventing their "unauthorized" propagation (a function of nature which unfortunately limits the resale market of an agribusiness concern) for the next growing season. Without even addressing the risks to wild crops that might occur as a result of Terminator gene flow, what appears to be an attempt to protect an innovation also overrides the rights of farmers, established through generations of practice, to plant next year's crops from the seeds that they grow. These conflicting rights can only be addressed in a rights-based model of IP.

In the post-genome world, IP decisions are clearly about much more than stimulating and rewarding innovation. They are also about accountability, control and governance. In biotechnology, these decisions determine not only who will own emerging technologies, but also influence how much they will cost, to whom they will be available, who controls the direction of their development, what kinds of institutions and values will guide technological choices, and what aspects of the process will be transparent to whom. These aspects of the politics of IP became visible in the 1990s, producing a new set of challenges for institutions of governance.

The significance of this transformation has yet to be fully appreciated, but Hilgartner asserts that it is quite possible that the challenges surrounding IP will come to rival those surrounding risk. We would go a step further and say that the challenges surrounding IP are central to the risk equation. Innovation-centric IP laws simply cannot reconcile the tensions between the various stakeholders, while rights-based framework IP laws automatically broaden the discussion to include virtually all the critical issues (and actors) which inform today's debates. Shifting to a new rights-based system will also necessarily cause shifts in other, connected institutions, as

discussed in the risk section above. But these shifts are likely to be the only means for developing a concept of acceptable intellectual property that ensures more equitable participation in policy making and addresses the deeper political issues of this new and increasingly vital domain at the intersection of economics, law and science.

[4.3] Genetic identification and informed consent

Outside of the research lab or the rice field, there are various legalistic ways in which various stakeholders are attempting to mitigate risks posed by the existing, innovation-based system for intellectual property rights. One of them is by employing the notion of “informed consent”, which is primarily concerned with obtaining the rights to medical samples and the information derived from them (although it might gain relevance in the previous discussions of plant engineering as well).

Informed consent has, for more than a decade, been a staple of the European Union’s approach to protecting its citizens’ privacy and personal data. Unlike the United States, which has historically fought hard to maintain the rights of commercial enterprises to collect, own and use certain types of personal data without obtaining permission, since the early 1990s the EU has taken a proactive stance on protecting data confidentiality via informed consent. The principle has various legal definitions in various countries, but as a general rule, informed consent means that no one — including commercial firms, research institutions and/or the government — can collect or process certain types of data about individuals, no matter where or how they get it, without first gaining explicit consent from that individual, disclosing precisely what they will use it for, and providing access to the information.

Two of the most notorious historical events that serve as the foundation for the process of informed consent were the medical “experiments” committed by Nazi doctors during World War II against Jews, and the Tuskegee Syphilis Study that was conducted by the U.S. Public Health Service for more than 40 years, starting in 1932, on several hundred black men in Macon County, Alabama. They were told only that they were being treated for “bad blood.” Once penicillin was discovered, treatment was withheld in order to collect data on “untreated syphilis.”

Studies such as Tuskegee prompted the formation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research by the National Research Act passed in 1974. The results of the charge of the Commission — to identify the basic ethical principles for the conduct of human research — were published in *The Belmont Report* in 1979. The Belmont principles are the foundation for the conduct of human research today, identifying three basic principles: respect for persons, beneficence, and justice. “Respect for persons” is the basis for informed consent in the research process, and is the requirement that gives research subjects the freedom of choice in determining what will or will not happen to them.³⁷

As it pertains to the collection of genomic material and the information it subsequently yields, the question is whether the Belmont principles will extend to genetic materials and information. The notion is more complex than it might seem. If we accept the idea that intellectual property is not created solely by innovation, then informed consent means more than simply “gifting” one’s tissue sample for research purposes and/or for “the good of humankind”, as one does today to donate blood; it must also include a discussion of post-research benefits and risks, whether financial or medical or both. In addition, collectors of genetic material and information — particularly those who attempt to collect an entire population of samples, be they from diabetics,

for example, or an entire nation/race of people (such as the DeCODE databases in Iceland) — want to be able to continue to use the information for further, possibly unanticipated analysis without recontacting the individuals for explicit consent.

This is known as “secondary use” of data, and is not generally supported by tissue donors. Also, there are implications for family privacy; once data has been collected on an individual, much of the same genetic information is de facto known about others in the family who may not have provided consent. Given the activity already taking place in this sphere, whether this constitutes “respect for persons, beneficence and justice” has yet to be decided.

Questions also arise regarding the definition of the term “informed”; that is, whether participation in an academic, medical or commercial project was truly voluntary, and not induced. A particularly interesting situation arises when a database of genetic material and information, gathered with informed consent for non-genomic research purposes by a university, for example, is subsequently sold to a commercial concern to be used for genomic research or some other purpose. If we think we are barraged today by “junk” mail, telephone solicitations and email “spam,” the ability to precisely identify individuals by their genetic material may well place us on the brink of the most sophisticated and invasive barrage of “targeted marketing” imaginable. (We are only partially joking about this.)

[4.4] How personal is genetic information?

One metaphor that has been used to describe the uniquely and highly personal nature of the genetic information yielded by DNA is that of a encoded “future diary.”³⁸ Diaries are generally considered to be deeply personal documents — private, truthful, usually hidden and locked to ensure privacy. While traditional diaries describe the past, however, the information spelled out in one’s genetic code can be thought of as both a personal history of inherited traits and a coded probabilistic future, the knowledge of which (depending on who knows it) may have a profound effect on an individual’s life possibilities.

Also unlike traditional diaries that are created by the writer, the personal information contained in DNA, which is stable and can be stored for long periods of time, is passed along in code and is largely unknown to, and certainly indecipherable by, the “writer”. Much of the code has not yet been broken by scientists, but new parts are being deciphered almost daily. As decoding techniques improve, as the cost of the technology continues to plummet, and as genomic biology continues to unlock the mysteries of how genes interact with other biological systems, if one’s DNA is deciphered without knowledge or permission, another person may someday be able to learn intimate details of an individual’s likely future health that even the individual does not know. (Although in terms of health, it is important to remember that in almost all cases genes do not entirely determine the development of a disease.) Thus even if today’s prevailing wisdom concludes that genetic information that can currently be derived from DNA analysis is no different from other sensitive medical information, *the DNA sample itself, with its ability to yield far more information in the future as genomic science develops, remains unique.*

Deciphering an individual’s genetic code also provides the same probabilistic health information about that individual’s family, especially close relatives like parents, siblings, and children.

Gleaning genetic information from the analysis of DNA (or proteins or other biochemicals closely associated with DNA) requires a sample that can be obtained from any bodily tissue: a mouth

swab, a few hairs or flakes of skin or a tiny spot of blood. It is the ability to base DNA or associated biochemical testing on these minute biological samples that makes the technology so powerful in crime detection (and also makes it so critical that the tests be accurate and properly conducted, and the samples uncontaminated, neither of which are certain today). But by the same token, it is very easy to obtain a sample for DNA testing from an individual without their knowledge or consent — from a coffee cup tossed into a public garbage bin, for example, or a discarded Kleenex, or a bit of dandruff or shed hair off the shoulders of a jacket or chair.

Given the amount of information that a snippet of human tissue can provide, it is not surprising that once informed, some tissue donors might want to keep track of what their “donated” DNA is being used for. In the United Kingdom, for example, the Human Genetics Commission (HGC), which advises ministers on issues in human genetics, recently published comments responding to the House of Lords Report on Genetic Databases that noted a “clear response” from a commissioned “People’s Panel” survey (published in March 2001) that new research should require fresh consent. It also recorded general opposition to the idea of an “opt-out” (otherwise known as “presumed,” or assumed consent) from particular types of research.³⁹

The ease by which virtually anyone with the will to do so can gain access to this most personal information creates many risks to privacy and civil liberties which bear serious consideration. For example, genetic information and misinformation has been used by governments (most notably in Nazi “racial hygiene” policies) to discriminate against those perceived as genetically unfit, and to restrict their reproductive decisions.

[4.5] Who owns the “rights” to your genetic profile, and to what end?

Genetic databases are being snapped together in the United States today with little discussion regarding the eventual disposition of samples or data once they are collected. In the U.S., people seem more willing to part with this most personal property — and are less informed or warned of the consequences — than they are with their credit card or telephone numbers.

Although some form of informed consent is often required for genetic testing on adults, newborn screening is the only mandatory genetic testing in the United States and most other countries. The ethical rationale for making tests mandatory instead of voluntary is that the State has the obligation to protect its most vulnerable citizens from harm; since newborns cannot give their own consent for testing, the State assumes the role of “*parens patriae*”, or beneficent parent. In 1998, only two states required written informed consent from a parent for genetic screening. All states except South Dakota allow parental refusal, but only five (and the District of Columbia) require that parents be informed of their rights to refuse — which, one could well argue, makes the ability to refuse somewhat moot.⁴⁰ But the larger questions remain: What happens to those samples, and the data they generate, after the initial tests are performed? Who owns them, and what will they do with them in the future? What will stop those who control the data from using it to deduce information about the parents or other family members — to perform paternity tests, for example, or other types of unauthorized screening?

In the adult population, the risk of losing access to health insurance due to negative genetic test results has spurred 42 states in the U.S. to enact laws that provide some level of protection against discrimination in this area. But broad public debate on these topics is almost non-existent, particularly in comparison to Great Britain, which has been much more proactive in assessing public attitudes about the various uses of personal genetic information (although it

rather enthusiastically collects such information, regardless of debate). As the result of an extensive study, the U.K. Human Genetics Commission has not only recommended a moratorium on using genetic test results to calculate insurance premiums, but also recommended that insurers give more information about how premiums are calculated, especially where family history information is being considered. The commission also noted that while the burden of “utmost good faith” — the main principle underpinning private insurance contracts in the U.K. — rests primarily with the applicant, the “increasing presumption across society in favor of greater openness and transparency in this area” should be noted by insurers whose access to genetic test results grants them far greater power to grant or deny coverage.⁴¹

[4.6] The DeCODE saga

Those interested in the impact of governments’ actions regarding personal genetic information are also closely monitoring the unfolding of the DeCODE Genetics saga in Iceland. DeCODE, which operates in Iceland but is incorporated in the state of Delaware in the U.S., is constructing three vast databases of individual Icelanders that will operate separately as well as in combination. First is a genealogical database of the Icelandic population for most of the last millennium. Second, a genetic database of DNA sequence and other information produced from blood samples is currently being collected by DeCODE in collaboration with a few physicians and medical organizations. And third, a database containing past, present, and future medical records from every Icelander, living or dead, produced from the nationalized system of health care, and usually referred to as the Health Sector Database (HSD).

According to Michael Fortun of the Department of Science and Technology Studies at Rensselaer Polytechnic Institute, and one of the most prolific (and outraged) chroniclers of the DeCODE saga, the company manifests virtually all the issues of global concern regarding human genetic research, including questions of informed consent, the privacy of medical records, ownership of and access to biosamples, and the future uses of genetic information.

The Icelandic government has granted DeCODE an exclusive 12-year license for the Health Sector Database, and it is this database that has drawn the most criticism. The HSD is to be constructed on a principle of “presumed consent” rather than informed consent. That is, by national law, the medical records of every Icelander living or dead were included as part of the database population without asking their explicit permission. (How that law was passed is a story itself.) Those still alive can fill out a form to get taken out of the database; they have no choice about being included in the first place. If an Icelander changes his or her mind later, the information cannot be withdrawn. Two years after the Act was passed, more than 19,500 people (out of a population of 280,000) had opted out of the database, with their numbers continuing to grow slowly but steadily.⁴²

Those with highly attuned personal privacy meters (or with slightly paranoid tendencies) may find it particularly disturbing that this list itself, the database of “opt-outs”, is as Fortun noted, “a kind of database of civil disobedience: an encrypted list of everyone opposed to this piece of government legislation and the private enterprise which it sanctions — with the coding key held by the government’s Director General of Public Health.” In other words, it is a list of people who do not want to be on a list. What might they have to hide?

To add to the social, ethical, and legal concerns, the blood samples that are being collected by DeCODE and its collaborating physicians to generate DNA sequence and mapping information

are being collected on the basis of “open” or “broad consent” — not for a specific research purpose or disease study, as accepted principles of informed consent require, but for any use that DeCODE decides to pursue at any time in the future. Fortun claims there is at least one documented case, involving a person with multiple sclerosis, where DeCODE has repeatedly refused to return the biosample and destroy all data, as this person requested.

According to Fortun, genomics researchers in many countries, including the U.S., are trying to relax the protocols of informed consent in a similar manner, arguing that the risks to research subjects are minimal, and that it’s too burdensome in genomics research, where thousands and even tens of thousands of samples need to be analyzed and compared, to require a researcher to get informed consent from each sample donor for each new biomedical study undertaken.⁴³

[4.7] The precautionary principle, and the risk of vague definitions

No discussion of post-genomic risk and governance would be complete without addressing the “precautionary approach” for international biosafety, although frankly it is an area where angels rightly fear to tread. Its contentious history is something of a textbook case of why it is so difficult — and so critical — to find a new way to deal with scientific risks and how they are assessed and acted upon by a large and varied group of stakeholders, all of whom have various outspoken and unspoken agendas.

As mentioned earlier, the precautionary approach of doing no harm is the defining objective of the Convention for Biological Diversity (CBD), one of the outcomes of the historic United Nations Conference on Environment and Development (also known as the Earth Summit) held in Rio de Janeiro, Brazil, in June 1992. The Convention has been ratified by more than 170 countries, including the United States (however, the Cartagena Protocol for Biosafety which was adopted to the Convention in January 2000, has not yet been ratified by the U.S.). The precautionary approach was codified in Principle 15 of the Rio Declaration on Environment and Development, which stated that “In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.”⁴⁴

It is from this broadly defined departure point that the battles begin. There are hundreds of documents on the web devoted to arguing the possible shades of meaning and repercussions of implementing the precautionary principle. One of the key conflicts, insofar as one is discernable amidst the noise, seems to be a fairly high level of ambivalence about lessening our international reliance on scientific certainty for proving risk, and allowing “other” (i.e., non-scientific) precautionary factors to influence risk assessment. But when the risks and adverse effects are still largely unknown, and when some of the potential risks stand to be irreversible, how does one gauge an acceptable level? What other factors can rightfully veto an action in the face of scientific uncertainty (or even scientific certainty, for that matter)? And in the light of such uncertainty, how can useful scientific and economic progress not grind to a complete halt?

This is the first time in history that we have had the luxury — albeit not for long, considering the gravity of the potential risks — where we have both the collective wisdom and a little more time to effectively debate these issues. Enough information is now known, and we are not presently in the midst of such crisis that it is impossible, to begin a methodical discussion to attempt to answer these questions, particularly given the relatively recent sequencing of various genomes

and the subsequent increase in biotechnology products and genetically modified organisms which are moving as quickly as possible to market.

The recently adopted (January 2000) Cartagena Protocol of the CBD is an overt acknowledgement of these new risks; the objective of the protocol is “to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements.”⁴⁵ The issues addressed by Cartagena have taken on even more urgency with rapidly growing fears about bioterrorism and the unanticipated migration of living, genetically modified organisms through crops and other ecological systems.

And while various academic strategists and policy are debating “science versus precaution,” the World Trade Organization (of which the United States is a powerful member) is moving forward its own agenda with the TRIPS intellectual property accord, passed in 1994 and touted by the WTO as “the largest trade negotiation ever, and most probably the largest negotiation of any kind in history”.⁴⁶ TRIPS appears to be the diametric opposite of the Cartagena Protocol: an engine for the growth of an international biotechnology marketplace based on the principle of innovation-based, rather than rights-based intellectual property, whereby living modified organisms are treated as discrete fungible commodities, tradeable across borders, without explicit acknowledgement of the various social and cultural networks and concerns that have been discussed here so far. These issues will either be decided by political operatives and lobbyists, or they will be decided by a larger circle of stakeholders. That is the choice with which we are presented.

[5.0] Taking action: enlarging the conversation

Despite the unprecedented nature of many of the outcomes, both known and unknown, that may become manifest in a post-genome world, there are precedents for dealing with at least some of them. These precedents have primarily been concerned with enlarging the conversation in a variety of ways —by expanding the number of stakeholders involved in the discussion process by which risks are analyzed and determined, by looking at longer time frames for risk, by increasing the number of perspectives (including precaution) which are considered as integral to the discussion/analysis, by challenging scientific objectivity as the only measure of risk.

In an article on science and the precautionary principle, Philip Bereano of the University of Washington's College of Engineering refuses to separate the notion of risk from precaution. "Even a rigid determination of a clear risk — say of injury from skydiving — cannot tell us why only some people will agree to jump from an airplane. We must recognize that risk itself (defined as the probability of a hazard) has subjective elements."⁴⁷

These subjective elements include the choice of phenomena to research; the definition of what constitutes a hazard; how to actually measure a hazard, especially if it combines different aspects not subject to a single metric (e.g., the death of a bee deprives us of both honey and pollination); how to account for incomplete knowledge; who has the burden of proof of developing the necessary data; how to account for the social distributions of risk, since hazards impact different sectors/classes in society differently; how to discount future events in light of present actions (will an endangered species be driven to extinction before the recovery efforts might be mounted); how to monitor a risk, and how much such surveillance is "worth" in both monetary and non-monetary terms; and so forth. In some measure, this is the definition of the precautionary principle.

Despite the logic of Bereano's observation that precaution is already integral to scientific risk assessment, the dominant view remains that assessment is a matter for "sound science" rather than politics or social values; these other messy forces must wait until after the risk is assessed. Then they can come into play as part of "risk management."⁴⁸

[5.1] Decision analysis: a tool to calibrate unknown risks?

Thus one of the most useful additions to the discussion would be an effective method by which to quantify the subjective or unknown scientific, economic and legal/societal risks noted by Bereano, as well as others mentioned in the previous sections above. The information that is used to build actuarial models of probability, for example, is derived from many disparate sources, including recorded observations of human behavior. But key is the ability to first identify a risk, then to have some means by which to both quantify it and contextualize it. This is a particularly difficult problem for any kind of standard determination of the risks of genomic biology, since the risks are largely unknown: there is no population of comparable cases where actions and outcomes can be tabulated, and probabilities calculated and compared with familiar values.

As Benjamin Kuipers, a highly regarded computer scientist at the University of Texas, recently commented on the public perception of risk and the anthrax crisis, "A presentation of risk

requires probabilities, but those numbers are meaningless unless calibrated against a standard spectrum of risks that people are familiar with. ... Uncertainty and the changing state of knowledge require not just probabilities, but ranges of probabilities.”⁴⁹ Considering the dearth of historical data and the nascent state of knowledge regarding the potential risks of experimentation with genetic material, then, today’s standard risk models do not yet have the data to adequately identify, quantify or contextualize post-genome risk probabilities.

This is not to say that a method that might begin to quantify all these subjective risks and probabilities is a panacea. That said, any method that could help weight and calibrate subjective probabilities, that could provide an alternative context for viewing these probabilities, could be a powerful tool to augment a daunting job for stakeholders and decision-makers.

A method with some promise in this realm is called “decision analysis,” a mathematical method for analyzing a broad and complex range of data which includes observations, information, and unknown possible events. Various research groups have implemented highly-sophisticated expert-system computer programs applying the decision analysis method to problems in particular disciplines. Kuipers, in a recent conversation, posited that decision “trees” might be able to provide the starting point for a structured approach to address the deep complexity inherent in trying to quantify the unknown risks of new genomic technologies.⁵⁰

Building a decision tree begins with the subjective, qualitative process of brainstorming about all possible risk-benefit scenarios, then trying to capture a “tree” of these possible futures, where a “branch” point represents either a set of choices or a set of “chance” outcomes. Next is the task of estimating the probabilities of the branches, with the outcomes at the leaves of the tree. In the post-genome world, where the risks are largely unknown, Kuipers says, “this is hard, but these are more focused problems than trying to deal with the issue as a whole.” A decision-tree program also allows for what Kuipers calls “meta-reasoning”, where tree-builders can criticize the structure of a tentative decision-tree, and evaluate how sensitive the result is to the assumptions they have made.⁵¹ A gut reaction that the result is not plausible can lead to deeper thought, new branches in the tree, revised assumptions, and a better decision tree.

Kuipers warns that decision trees cannot capture the full complexity of the unknown risks of new genomic technologies by popping out a simple number that estimates unknown risks. After all, as any good computer programmer knows, it is easy for an unexpected error to lurk deep inside the structure of a sophisticated program, the code for which may need to be deconstructed, perhaps many years and many faulty “decisions” down the pike. But, Kuipers adds, with this in mind, “You can [still] get a richer understanding of the tree of possible futures, and the good and bad scenarios available after taking any particular branch.”⁵²

There are no doubt several existing projects, and one would hope many qualified artificial intelligence experts who could be convinced to take on the challenge of creating a decision tree that would address the vast complexities of post-genome risk. One possibility is a project underway in the Clinical Decision Making Group at MIT’s Laboratory for Computer Science (LCS). Intriguingly, this group is exploring ways in which decision analysis software can “attend to a broad range of observations, information and actionable conditions that cannot be enumerated beforehand”, which is a fairly good description of the post-genomic risk continuum.⁵³

One of the project's directors, Peter Szolovits, warns that there is "no magic" to the approach. Although decision analysis techniques have been applied in many different areas, including clinical decision making, business risk analysis and public policy — places where there are uncertain risks or benefits to be compared, or trade-offs to be made — common sense is still required to apply its methods appropriately. "The kind of problem I have been interested in is one where the possible actions and consequences are not drawn from a small fixed set," wrote Szolovits in a recent email. "However, it is still critical to have some theory that can, in any particular instance, derive those."⁵⁴

For example, says Szolovits, he is presently working on a project that requires an a priori estimate of the likelihood that an individual arriving at an Emergency Room has been the victim of bioterrorism. A tiny likelihood, but in a post-9/11 world, how does one make such an estimate? Apparently by bounding the question wisely; i.e., "if a patient is the victim of bioterrorism, which agent is most likely to be the cause", which can be answered somewhat more independently of the underlying likelihoods of attack.

[5.2] Expanding authority beyond the realm of science

Because questions and alternatives are so often determined by point of view — i.e., a laboratory scientist will present a very different set of alternatives from, say, a politician, or a lawyer, or an indigenous land owner in Brazil — making tools such as decision analysis useful in the post-genome world, with its exponentially higher levels of complexity, would seem to require input from a much-expanded base of these knowledgeable stakeholders.

In addition, again according to Kuipers, it is difficult to know, when one is building a decision tree, whether some branches have been left out. Thus, he says, the storytellers of our culture might assume a critical role in helping us think about post-genome risk. Kurt Vonnegut once said that science-fiction writers are the most important writers of the age. Kuipers says this is because "science fiction writers consider the implications of new technologies on society in ways that few other thinkers do. The future world laid out by a science fiction writer is the result of a path through the decision tree we want to construct, taking one set of choices and chances as it passes through the nodes in the tree."⁵⁵⁵⁶

By using their thinking about that fictional world and its fictional history, says Kuipers, decision-tree analysts can infer what some of the real nodes are in the decision tree, and what other branches it might have. "Then we can apply our best judgment to determining the probabilities associated with the chance nodes." This may sound like a flight of fancy, but some of them have been around long enough to see some of their "flights of fancy" come to pass. As a result, it has become common practice for many well-known science fiction writers to make presentations to future-hungry groups ranging from the Bioneers Conference to the U.S. Central Intelligence Agency.

Kuipers agrees with Szolovits's assessment that having a theory regarding actions and potential consequences of risks is critical for making good use of decision analysis. Even creative brainstorming with stakeholders to define some set of possible outcomes, then try to assess the orders of magnitudes of the probabilities, could be too much to ask. For example, he writes, "What is the probability of the escape of a highly virulent infectious virus carrying something that will modify germ-line cells in humans, and thereby destroy or modify the entire human race?"

The utility is obviously very low, but so is the probability. If it's 10^{-10} , I might still worry, but if it's 10^{-100} , I probably wouldn't worry."⁵⁷

It is always possible that the worst risks are the ones that no one considered. Nonetheless, it seems sensible, if not valuable, to at least start the process of tabulating and considering all the risks that have been considered. "For one thing," writes Kuipers, "this provides a baseline so that different people can contribute their ideas to a common pool of possibilities, thereby increasing the number of scenarios that are seriously considered."⁵⁸

[5.3] Processes, and manifestos, for transparency

Somewhere between the useful theories of mathematical probability and the equally useful fictions of storytelling are organizations who are in the field with actual human beings, doing the pick-and-shovel work of developing communication processes to increase openness, public participation and transparency in making decisions about complex issues, particularly those involving science and technology. In democratic societies, at least, this focus on openness and transparency is considered especially important because the knowledge required to understand scientific and technological issues is sufficiently arcane that is difficult to communicate to politicians or citizens without concerted effort or considerable bias.

One of the most prolific organizations in this area is a Swedish group called Karinta-Konsult. This consultancy — which exists primarily in the person of Kjell Andersson, a theoretical physicist who served as a systems analyst for the Swedish National Defense Research Institute as well as the Swedish Nuclear Power Inspectorate — often publishes and works in collaboration with university professors Clas-Otto Wene, a professor in energy systems technology from the Chalmers Institute of Technology in Goteborg, Sweden, and Raul Espejo, a professor of information management at the University of Lincolnshire and Humberside in the United Kingdom. As a team, they have conducted several public and private projects, all of which center upon developing models for transparency and improving decision processes for complex issues. The models originate from work in nuclear waste management, but could prove equally relevant in other areas where science and technology spawn complicated risk scenarios.

Key to all the models is an acknowledgment of the limitations of the "expert" role, or agenda, in complex scientific or technological decisions. This agenda, says Andersson, has worn thin as the complexities and radical risk possibilities of new scientific discoveries are brought into direct contact with the public who must shoulder them, and the governments which are supposed to protect them. He cites several anomalies in the "expert-agenda" system which provide a good summation of why the "expert" method for risk assessment may be forced to undergo a shift toward transparency:

- **Experts** are supposed to be objective, but they are often (some go so far as to say "always") captive to their own underlying values and conflicts, both in the framing of the original research and the assessments they later make regarding research. Also, they often have strong positions, and for various reasons may have a vested interest in the status quo.
- **Politicians** are supposed to guard the interest of their voters, but the quality of the decisions they make are based on information provided to them by experts; in addition, they are exposed to pressure from lobby groups who can leverage

the vast amounts of information to fragment various arguments. Also, they are often under inordinate time pressure to learn more about the subject before they have to make a decision.

- **The public** is supposed to be well informed, but is overloaded with information, and have few opportunities for quality review of the information they receive. The Internet does not solve the problem, but rather adds to the information overload.
- **The media** are supposed to act as agents of review for the public on these issues, but are subject to the vagaries of the media marketplace, are subject to lobbying and have limited resources for in-depth analysis.⁵⁹

In what will no doubt be a controversial document called the VALDOC Manifesto, Andersson and an international, interdisciplinary group of scholars have outlined a set of procedures designed to produce a public discourse which counters the above anomalies and sets up a new paradigm for public discourse on complex issues.

The manifesto states that any new procedures or arenas for such discourse must meet the following nine conditions:

1. A multiperspective starting point;
2. The capacity to evaluate claims of truth;
3. The capacity to evaluate claims of legitimacy;
4. The capacity to evaluate claims of authenticity;
5. The capacity for “stretching,” or opening the minds, of stakeholders to new and alternative issues and perspectives;
6. Impartiality (i.e., ideologically and politically neutral);
7. Publicity and appropriate access to media;
8. Representation by diverse perspectives; and
9. Access to leaders, with participation by decision-makers.⁶⁰

One can imagine the precepts of this manifesto being used to help develop risk scenarios as branches and nodes in a risk analysis which employs the decision tree, as described above.

The Karinta group is not alone in re-examining the role of scientific advice in risk evaluation, and suggesting new approaches. In a report for a workshop on risk management sponsored by the European Science Foundation, Chris Elliott, a systems engineer and barrister who holds a visiting professorship at the University of Bristol, summarized a lengthy research project on the proper governance of science and technology prepared by Oxford Economic Research Associates Ltd for eight government bodies in the United Kingdom. His report, called “Scientific Uncertainty, Technological Risk and Public Policy,” also proposes a useful, more inclusive framework for making decisions about risk.⁶¹

In an argument that echoes Beck’s, above, Elliott claims that the proper governance of science must accommodate two views: one, that science is uncertain, and two, that technology can never be risk-free. The key to making this accommodation is a method by which decisions on matters of public safety can be made in a way that is rational, defensible and equitable. Any rational, defensible and equitable decision on matters of risk must then address two questions: How great are the benefits and dangers? And do the benefits outweigh the dangers?

In order to answer these questions, a disciplined approach to assessing scientific uncertainty, which includes the rights of stakeholders and participation by both policy makers and decision makers, is required. In this, Elliott's argument echoes many of those found in the Karinta construct above. Notably, he acknowledges that scientists ("experts," in Karinta's model) are not independent and should only be expected to be honest about and disclose their biases. He also states several key areas where stakeholders other than scientists should contribute to the decision making process, particularly where the potential benefits of a decision do not fall to the same stakeholders as those who might suffer.

The framework that results from this disciplined approach to risk has been dubbed ALARP (As Low As is Reasonably Practical), with of course the devil being in the definition of "reasonable" and "practical." Within this framework, several principles form the foundation for how government obtains and uses scientific advice, and should lead to more legitimate and democratic behavior by governments around policy issues which require scientific advice. Their key consequences are:

- The risk decision will be made by an appointed person in government who is then responsible for that decision. The decision will not either expressly or implicitly be usurped by scientists;
- Those on whom the consequences of the decision (both good and bad) will fall will influence the decision, not the scientific advice;
- The scientific advice will be provided by people with the correct expertise, without necessarily requiring them to be independent.

Although Elliott claims the framework still requires subjective judgment to implement, and will be difficult to translate into a legal culture based on civil law, it does provide a way for decision makers to begin structuring their thinking and ensure that, even when it is necessary to be subjective, the lines of argument are clear and may be reproduced and reviewed, if new information or requirements were to emerge. Some in British government seem to concur. In a recent conversation, Elliott noted that the U.K. Health and Safety Commission, one of the report's sponsors, adopted the OXERA report conclusions wholesale in its response to the lengthy government inquiry regarding Bovine Spongiform Encephalopathy (BSE), or "mad cow disease".⁶²

In the case of risks posed by advances in genomic biology, and which are thus unique, and unanticipated, the challenge to make a decision which is "rational, defensible and equitable" is much more complex because the decision must be made in the absence of certain knowledge of the potential hazards (i.e., "acceptable levels"). However, Elliott concludes, the proper governance of science and technology demands an approach that imbues the full complement of stakeholders with some degree of power if such risks are to be properly managed.⁶³

[6.0] Who can you trust? Suggestions for a new approach to governing risk

In the ALARP model, there is a clear distinction between the roles of decision makers and policy makers. Where the decision maker has the actual authority to write a law or create policy (which is not precisely the case in the United States; even regulatory agencies must report to Congress), the policy maker's role is to help the decision maker reach a decision, either by providing analysis, generating options or conducting risk assessment, in part by calling on scientists to help inform these decisions. Thus policy makers are at the nexus of the process. The difficulty in the post-genome world is to find a policy maker who is sufficiently trusted by all parties to provide such input, particularly given the conflicts posed by the confluence of scientific, economic and legal interests in maintaining the status quo.

[6.1] The case for a 'boundary organization'

Although there have been some examples of such policy makers in the past for various other purposes, none such exist today for the governance of the post-genome world. One possible alternative to consider for post-genome governance is the creation of what are known as "boundary organizations" which exist at the intersection of science, politics and the public interest. David Guston, a professor of public policy at Rutgers University, calls boundary organizations a "newly minted analytical concept" with intellectual ties to both the sociology of science and the economics of organizations that have proven useful in various capacities in the recent past.⁶⁴

One such example is the U.S. Congressional Office of Technology Assessment, which was voted out of existence by Congress in 1995. A widely respected, politically neutral agency — called "a natural treasure" by many — for 23 years OTA assisted Congress with the analysis of policy problems with high technical content. It maintained its neutrality — in fact, its neutrality was enhanced — because it was equally accountable to Democrats and Republicans, as well as to various Congressional committees with overlapping or competing jurisdictions. Guston, who once worked at the agency, says it internalized partisan differences, negotiated them for each of its studies, and consistently produced credibly nonpartisan work that anyone could use for their own purposes.⁶⁵

Also appropriate to this discussion might be the International Research Institution for Climate Prediction, housed at Columbia University. The Institute engages in what it calls "end-to-end" climate research, from modeling the physics of climate change, to forecasting precipitation and temperature, and helping people and organizations make use of the information it generates. Guston, who is one of three researchers who has studied the Institute's strategy as a boundary organization, says its job is somewhat complicated by the fact that it is operating at the edge of knowledge as well as between the developed and developing world, as would be any boundary organization managing the process of redefining risk in the post-genome world.⁶⁶

[6.2] 'The Office of Biological Policy Assessment'

So what might such an organization — call it the Office of Biological Policy Assessment — look like? Given that we know the possibility of scientific risks exist, but we cannot yet know if, when or where they will appear, a post-genome boundary organization might address the rich menu of policy issues that would be raised by tracking or monitoring areas around the world where hazards might manifest themselves, researching and developing policies to protect individual privacy, cultural diversity and the environment.

As an example, with input from all stakeholders, it might eventually recommend the formation of a kind of nongovernmental Bio Peace Corps, where young scientists are trained and head out into the field for several weeks or months to sample salmon populations or crop yields for gene flow, or monitor water supplies for active genomic compounds. Such a group might also be able to assume a non-governmental role in national defense role as well, as a “Biological Defense Command” that monitors the environment for “incoming” biological agents, behaving similarly to NORAD, the North American Aerospace Defense Command that’s charged with aerospace warning and aerospace control for North America.

Such a boundary organization might also take on the task of analyzing the potential of a process such as decision analysis, informed by the Karinta or Oxford processes to include the more subjective risks of genetic testing, DNA databases and others as discussed here. With equally weighted input from all stakeholders, it might propose a global protocol for the proper conduct of genetic tests, and dispensation of results. It could analyze the risks inherent in various intellectual property regimes, and experiment with test beds and alternatives for policy and regulatory changes that would not unduly disrupt the market, but would allow scientific progress to co-exist with various stakeholders’ declared needs for intellectual and cultural autonomy.

It could provide unbiased reassessment of the benefits of existing laws such as the Cartagena Protocol and the TRIPS accord, the Bayh-Dole Act and the Belmont Report, and others that have and will affect outcomes in the post-genome world, informing the creation of laws that are acceptable to a wider constituency than today. It could study various issues around long-term stewardship of potentially harmful bioactive substances, and monitoring of the environment and living beings, particularly humans, who are subject to yet unknown genomic risks. It could attempt to broadly define the public interest and the public domain in a way that delivers the greatest good for the greatest number.

Whether such an organization should be public (i.e., part of the government, as was the OTA) or private, and why, are key questions to consider should this strategy be pursued.

[7.0] Conclusion: Ethics is not a separate conversation

The idea of a boundary organization is somewhat paradoxical; connecting institutions by an intermediary that holds firm the boundary actually decouples actors from the conflicts that occur when they come together out of shared necessity — as has been true, for example, with the hybrid research networks formed by universities (which needed money) and industry (which needed brainpower and ideas). Boundary organizations are oddly analogous to why good interdisciplinary research is so effective. When the stakeholders are invited to present their views, but must communicate about their work in a way that everyone at the table can understand, they create a kind of demilitarized zone where no one's views are eliminated, but fresh ideas and solutions are proposed which could never have occurred otherwise.

Until now, this paper has left the discussion of ethics virtually untouched — odd, perhaps, considering that any topic involving genomics now seems to sprout ethicists like mushrooms. That is because ethics as they are practiced today have been a separate conversation: too detached from the issues, too bonded to a specific actor (thus co-opted to some degree), or too prone to making grand pronouncements out of context of the complexities of the real world, which only continues to unhelpfully polarize the debate. It is helpful to note that bioethics in the world of the genome came to pass because one of founders of the Human Genome Project, James Watson (the co-discoverer of DNA), created the Ethical, Legal and Social Implications (ELSI) offshoot of the genome project specifically and admittedly to pre-empt critics of the project.⁶⁷

Klaus Hoyer, a Swedish medical ethicist writing about this issue in relationship to the gift economy and informed consent, observed while attending a conference on genetics that discussion of ethics in the scientific community literally took place in a room of its own, and scientists did not attend. Either one works on ethics or on science; the two are independent. Like the precautionary principle, ethics had become an extra — an option, rather than the Hippocratic foundation of the trade.⁶⁸

So perhaps the most appropriate metaphor for a boundary organization that manages ethics and acceptable risk in the post-genome world is that of an open house, as suggested by Michael Fortun, who says it may sound congenial, but by no means is it an innocent metaphor. Who does one invite in? Do the stakeholders at the fringe, with the most extreme views, get to clink glasses with each other, or are they even willing to try? Do giant multinational corporations that want to “go fishing” for potential disease genes and their potential therapies swap stories with those who believe in the absolute right for indigenous people to preserve their genetic ecology? How do we have an open house and still have a necessary measure of privacy, or maintain our proprietary interests?

If those are in fact the real ethical questions, then the metaphor of the open house is not only appropriate, but critical to any meaningful reassessment of risk. The challenge is to keep the door open, and invite in as many people as possible — from biologists to politicians and ethicists, from citizens and artists to farmers and biotech executives — with everyone engaged in the conversation, listening, questioning, responding. “Ethics is about remaining open to the Other,” says Fortun, “which also means remaining open to the future, which means remaining open to what you don't know.”⁶⁹

In such an open house, ethics will no longer be isolated from the conversation, but would be given the opportunity to spring organically from it. Science and technology may be at a critical inflection point and the fruits of their labors may be both unprecedented and historic, but they are not themselves revolutionary forces. They are part of an unfolding dialog, a continuum, and always have been. Genomic biology, revolutionary as it might be at this stage in its development, is even moreso. The nature of the world in which we live, with all its risk and promise, now demands that the Other be invited to join this conversation as well. Our task as a species, and as a body politic, is to understand these new risks and address them with all the sophistication that we are capable of bringing to bear. Accepting risk as a continuum will at last permit us to govern wisely, according to what may be the most basic truth of our time: that change is the only constant there is.

[8.0] About the Author

Denise Caruso is founder and executive director of the Hybrid Vigor Institute, a non-profit research organization that cultivates the sharing of knowledge and expertise for complex problem solving and applied research. Also a veteran journalist and technology analyst, Caruso for nearly 20 years chronicled the converging industries of digital technology, telecommunications and interactive media. From October 1995 until April 2000, she wrote the Technology column for the Monday business section of *The New York Times*. In January 2000, she became an occasional contributor to *The Times'* Arts & Ideas section, writing primarily about scientific and academic research in progress. Caruso was one of the earliest advocates of First Amendment rights in cyberspace, and one of the first journalists to focus on technology, commerce and culture. She serves on the Board of Directors of the Independent Media Institute in San Francisco, and the Board of Trustees of the Molecular Sciences Institute in Berkeley. She is an advisor to the Center for Public Knowledge and Consumer Web Watch, and is a board member emeritus of the Electronic Frontier Foundation. She can be contacted at caruso@hybridvigor.org.

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